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STUDIES ON PORPHYRIA

II. A CASE OF PORPHYRIA ACCOMPANIED WITH EPIDERMOLYSIS BULLOSA, HYPERTRICHOSIS AND MELANOSIS

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Porphyria is a constitutional state marked by the excretion of porphyrins, either in greater than physiologic amounts or of kinds not normally demonstrable. Clinically it presents two widely different pictures: the acute, with dynamic ileus and peripheral neuritis, and the congenital, with cutaneous manifestations.

Since Linser [1] in 1906 first recognized the repeated simultaneous occurrence of porphyria and hydroa aestivale, considerable attention has been accorded this association. The facts that hematoporphyrin was then thought to be the porphyrin excreted in this disease and that it was soon shown to have remarkable photosensitizing powers [2] seemed to offer a ready explanation of the coexistence of the two conditions. It has been only recently that doubts of the validity of the early explanation have drawn attention to the fact that other dermatoses may be found with porphyria. The present study concerns such an association.

CHEMICAL CONSIDERATIONS

Porphyrins are widely distributed, both in animal and in plant life, in hemoglobin and in chlorophyll, respectively. It may be said that chlorophyll plays no measurable part in the porphyrin metabolism of animals, and can therefore be disregarded in the present connection.

The animal porphyrins are red compounds which fluoresce red in ultraviolet light. In acid solution they have a three band absorption

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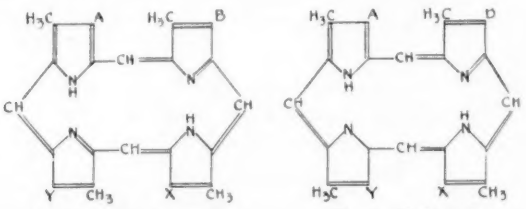
1. Linser, P.: Ueber den Zusammenhang zwischen Hydroa aestivale und Hämatoporphyrinurie, Arch. f. Dermat. u. Syph. **79**:251, 1906.

2. Hausmann, W.: Die sensibilisierende Wirkung tierscher Farbstoffe und ihre physiologische Bedeutung, Wien. klin. Wchnschr. **21**:1527, 1908; Die sensibilisierende Wirkung tierischen Farbstoffe und ihre physiologische Bedeutung, ibid. **22**:1820, 1909.

spectrum; in alkaline solution there are from four to seven bands. The precise position of maximum absorption of each band is characteristic for each porphyrin, but stereo-isomers can be distinguished only by determination of the melting points of the porphyrin-methyl esters. The important naturally occurring porphyrins are protoporphyrin, coproporphyrin and uroporphyrin, the structures and properties of which are given in figure 1 and tables 1 and 2.

It will be seen that there are two isomeric series of the coproporphyrins and uroporphyrins and that one of these is homologous with protoporphyrin. This protoporphyrin IX is the one whose iron complex bound to globin is hemoglobin. It is immediately important for an understanding of the problems of porphyria to realize that porphyrins



Protoporphyrin IX (Type III structure) A, B = CH = CH_2; X, Y = CH_2-CH_2-COOH

Coproporphyrin I / " III: A, B, X, Y = CH_2-CH_2-COOH

Uroporphyrin I / " III: A, B, X, Y = $CH(COOH)CH_2COOH$ *(probably)*

Fig. 1.—The constitution of the most important naturally occurring porphyrins (Fischer, H.: Ueber Porphyrine und ihre Synthesen, Ber. d. deutsch. chem. Gesellsch. **60**:2611, 1927. Maurer, H.: Farbstoffe mit Pyrrolkernen, in Abderhalden, E.: Handbuch der biologischen Arbeitsmethoden, Berlin, Urban & Schwarzenberg, 1933, vol. 14, no. 7).

of type I cannot arise from or give rise to porphyrins of type III,[3] for in this disease the uroporphyrins and coproporphyrins excreted are of type I, whereas protoporphyrin IX is of type III.

One caution should perhaps be uttered. Normally there is a daily excretion of coproporphyrin in both stools and urine, amounting to from 300 to 400 micrograms.[4] When one is seeking evidence of porphyria and reporting it this must be considered.

Protoporphyrin is insoluble in 10 per cent sodium hydroxide but soluble in chloroform and ether. The coproporphyrins are soluble in

3. Fischer, Hans: Ueber Porphyrine und ihre Synthesen, Ber. d. deutsch. chem. Gesellsch. **60**:2611, 1927.

4. Brugsch, J. T.: Untersuchungen des quantitativen Porphyrinstoffwechsels beim gesunden and kranken Menschen, Ztschr. f. d. ges. exper. Med. **95**:471, 1935.

10 per cent sodium hydroxide and in ether but insoluble in chloroform. The uroporphyrins are soluble in 10 per cent sodium hydroxide and in ethyl acetate at p_H 3.2 but are not soluble in ether or chloroform.

CLINICAL ASPECTS

There are on record approximately 200 cases of hydroa vacciniforme, about 86 of which there has been definite evidence of porphyria.

TABLE 1.—*Melting Points of Methyl Esters*

Protoporphyrin IX	219 and 235 C. †
Coproporphyrin I	251 and 214 C. *
Coproporphyrin III	145 and 172 C. *
Uroporphyrin I	311 ‡
Uroporphyrin III	258 §

* Fischer, H.: Ueber Porphyrine und ihre Synthesen, Ber. d. deutsch. chem. Gesellsch. **60**: 2611, 1927.

† Maurer, H.: Farbstoffe mit Pyrrolkernen, in Abderhalden, E.: Handbuch der biologischen Arbeitsmethoden, Berlin, Urban & Schwarzenberg, 1933, vol. 14, no. 7.

‡ Fischer, H., and Libowitsky, H.: Auftreten von Uro- bzw. Koproporphyrin I bei akuter Porphyrie, Ztschr. f. physiol. Chem. **241**: 220, 1936.

§ Waldenström, J.: Fink, H., and Hoerberger, W.: Ueber ein neues bei der akuten Porphyrie regelmässig vorkommendes Uroporphyrin, Ztschr. f. physiol. Chem. **233**: 1, 1935.

TABLE 2.—*Some Important Absorption Spectra of Porphyrins in Millimicrons* *

	In Tenth-Normal Sodium Hydroxide				
	I	II	III	IV	V
Protoporphyrin (6)	633	582	...	544	510
Coproporphyrin (6)	617	...	565	538	503
Uroporphyrin (6)	610	574	560	537	502.5

	In 25 per Cent Hydrochloric Acid			
	I	II	III	Ultraviolet
Protoporphyrin (6)	604	581	558.7	
Coproporphyrin (6)	592	548.7	491.3	402
Uroporphyrin (6)	596	577	553	410.7

	Methyl Ester in Chloroform					
	I	II	III	IV	V	VI
Protoporphyrin (6)	631	602	...	575	541	507
Coproporphyrin (6)	623	598	577	568	532	499
Uroporphyrin (6)	626	599	...	572	535	501

* These figures have been brought to the nearest whole number and represent the maxima of absorption.

In the majority of these the onset has been in childhood. When Günther wrote his monograph on porphyria in 1911 [5] he divided the cases of hydroa on the basis of age of onset into two groups, the congenital and the chronic. With increasing knowledge of the condition he came

5. Günther, H.: Die Hämatoporphyrie, Deutsches Arch. f. klin. Med. **105**:89, 1911.

to regard this separation as arbitrary and unnecessary,[6] a point with which we are in full agreement.

Our knowledge of porphyria has been built largely around studies on Mathias Petry, who was discovered at the age of 18 by Kuhnt[7] and studied almost continuously by various authors[8] until his death, at 32. A brief review of what was found in these studies may be attempted here for the information it throws on the disease.

When Petry was first examined, Günther[5] believed that his urine contained hematoporphyrin and a brown pigment to which he gave the name urofuscin. Fischer began the study of Petry's urine in 1915[9] and immediately showed that the porphyrin in the urine had an ester with a melting point of 296 C. (564.8 F.)—distinctly not hematoporphyrin. He suggested, therefore, that the disease be called simply porphyrinuria and the pigment uroporphyrin. The same year he obtained from the feces[10] another porphyrin which he called at first kotporphyrin and later coproporphyrin. Small amounts of this could be obtained from the urine.

Most of the pigment of Petry's urine was excreted as a colorless chromogen which yielded the porphyrin on oxidation. With this there developed much brown pigment. This was at one time thought to be a by-product of the oxidation of porphyrinogen, but on analysis no pyrrole could be found; it contained sulfur and on hydrolysis yielded amino acids.[9] In 1924 Fischer and Zerweck compared it with urochrome[11] and found it to be similar although not identical. They expressed the belief that urofuscin is a chromoproteid, although they made no mention of a chromogenic prosthetic group.

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6. Günther, H.: (*a*) Die Bedeutung der Hämatoporphyrine in Physiologie und Pathologie, Ergebn. d. allg. Path. u. path. Anat. **20**:607, 1922; (*b*) Hämatoporphyrie, "Die Krankheiten des Blutes und der blutbildenen Organ," Berlin, Julius Springer, 1925, vol. 2, p. 622.

7. Kuhnt, H.: Ueber symmetrische umschriebene Skleralnekrose bei Hydroa vacciniforme, Ztschr. f. Augenh. **27**:146, 1912.

8. (*a*) Fischer, H.; Hilmer, H.; Lindner, F., and Pötzer, B.: Zur Kenntnis der natürlichen Porphyrine: XVIII. Chemische Befunde bei einem Fall von Porphyrinurie (Petry), Ztschr. f. physiol. Chem. **150**:44, 1925. (*b*) Borst, M., and Königsdorffer, H.: Untersuchungen über Porphyrie mit besonderer Berücksichtigung der porphyria congenita, Leipzig, S. Hirzel, 1929.

9. Fischer, H.: Ueber das Urinporphyrin, Ztschr. f. physiol. Chem. **95**:34, 1915.

10. Fischer, H.: Ueber das Kotporphyrin: II. Mitteilung über das Urinporphyrin, Ztschr. f. physiol. Chem. **96**:148 and 309, 1915.

11. Fischer, H., and Zerweck, W.: Ueber den Harnfarbstoff bei normalen und pathologischen Verhältnissen und seine lichtschützende Wirkung, zugleich einige Beiträge zur Kenntnis der Porphyrine, Ztschr. f. physiol. Chem. **137**:176, 1924.

Günther [5] found that Petry was sensitive to ultraviolet rays, and Fischer [12] showed that mice and guinea-pigs given injections of uroporphyrin could be killed by exposure to sunlight. However, Hausmann [13] and Fischer and Zerweck [11] demonstrated that urofuscin would protect mice from the sensitizing action of uroporphyrin.

In 1915 Schumm demonstrated that the characteristic spectrum of uroporphyrin could be found in acid extracts of a piece of red bone removed from Petry.[14] This same spectrum was found in the bones of four swine with so-called osteohemachromatosis. This investigator examined Petry's blood spectroscopically and found large amounts of hematin and of porphyrin.[15] The spectrum of the latter agreed with that of coproporphyrin. The serum contained no methemoglobin, as it frequently does in cases of hematinemia.[16]

From 1915 through 1919 Petry excreted from 0.17 to 0.6 Gm. of uroporphyrin per day.[17] This gave the fresh urine a strong absorption spectrum: I 617-609; II 578-558; III 543-534; IV 515-476.[15] The excretion of uroporphyrin corresponded to an excretion of hemoglobin of from 2.9 to 10.3 Gm. per day, not including the excretion of coproporphyrin. This is an enormous pyrrole metabolism and by withdrawing pyrroles from the sources of hemoglobin must lead to anemia. This showed up in Petry's blood counts.[18] In 1919 splenomegaly was first noted.[17]

In 1923 Petry had a pleural exudate [18a] in which uroporphyrin was found and at the same time it was found in the serum as well. From that time on the patient was almost continuously in a hospital, and there was opportunity for Fischer and Zerweck to restudy his urine. They found [11] that with fever the excretion of pigments almost ceased. In the absence of fever they were able to demonstrate the appearance in the

12. Fischer, H.: Ueber die Giftigkeit des Porphyrins, Ztschr. f. physiol. Chem. **97**:109, 1916.

13. Hausmann, W.: Zur sensibilisierenden Wirkung der natürlichen Porphyrine, Biochem. Ztschr. **77**:268, 1916.

14. Schumm, O.: Ueber das "Hämatoporphyrin" aus Harn und Knochen, Ztschr. f. physiol. Chem. **96**:183, 1915.

15. Schumm, O.: Beiträge zur Kenntnis der Haematoporphyria congenita (H. Günther), und der natürlichen Porphyrine, Ztschr. f. physiol. Chem. **98**:123, 1916.

16. Bingold, K.: Hämolyse, Blutfarbstoffumbau, Blutfarbstoffzerstörung und Blutfarbstoffschutz. Zusammenfassende Darstellung eigener Untersuchungen, Folia haemat. **42**:192, 1930.

17. Schumm, O.: Weitere Untersuchungen bei Hämatoporphyria congenita: II, Ztschr. f. physiol. Chem. **105**:158, 1919. Fischer.[9]

18. (*a*) Weiss, H.: Zur Kenntnis der Porphyrinkrankheiten, Deutsches Arch. f. klin. Med. **149**:255, 1925. (*b*) Schumm.[17] (*c*) Günther.[5]

urine of other porphyrins than those previously described. These were not well identified, however. Further, there appeared in the serum both uroporphyrin and coproporphyrin and once a porphyrin which seemed to be intermediate between these two.[11]

At autopsy Petry was found to have died from bronchopneumonia. The tissues were turned over to Fischer for study, and the results of his work are embodied in a monograph,[8] of which we give a brief summary:

> The bones were red and contained large amounts of uroporphyrin. In the scapula, part of this was in the form of the copper complex (this is a red compound with a two band absorption spectrum, better known as "turacin"). The bone marrow contained protoporphyrin, coproporphyrin and uroporphyrin. Coproporphyrin was found in practically all tissues and was crystallized from the blood. In the blood there was spectroscopic evidence for the occurrence of coprohemin, but the substance was not isolated. The pleural exudate, the spleen and the liver contained uroporphyrin. In the spleen there was a large quantity of a brown pigment which contained no sulfur and was thought to differ from the brown pigment of the urine. The pale muscles contained no coprohemin.

Four years later Borst and Königsdorffer [8b] completed their pathologic studies on the tissues of Petry and published them in a remarkable volume of some 260 pages. In this they dealt largely with methods of fluorescence microscopy, particularly in relation to the study of porphyrins and hemins. They corroborated the findings of Fischer and his co-workers and found that the porphyrins were deposited in the tissues in various morphologically and chemically distinct conglomerates. By the analysis of these and in consideration of their spatial relations to various tissues they came to the conclusion that uroporphyrin and coproporphyrin are synthesized in the megaloblasts and that these are rapidly destroyed, liberating not only the porphyrins but brown pigment. They found that in fetuses and in subjects with pernicious anemia the megaloblasts apparently synthesize uroporphyrin and coproporphyrin.

In view of Fischer's demonstration (1) that Perry's porphyrins were of type I, whereas hemoglobin is derived from a type III porphyrin, and (2) that the one could not act as a source or a derivative of the other, Borst and Königsdorffer concluded from their own data that porphyria represents the persistence of a fetal stage of pyrrole metabolism which is entirely independent of and apart from normal hemoglobin metabolism.

Many cases similar to Petry's have been reported. A statistical analysis of the reported cases is, however, fraught with pitfalls. In the first place, the accompanying clinical manifestations may vary. In some cases there are atypical cutaneous manifestations or accompanying symptoms suggestive of the acute disease. In some it seems that the

disease is not congenital but acquired, as a result of chronic alcoholism,[19] of syphilis [20] or of some other cause.[21] Lastly, it is too often impossible to tell from the available data whether a patient had porphyria or whether the urinary porphyrin was not coproporphyrin in normal amounts.

Having carefully reviewed every available original paper on porphyria up to January 1936, we feel that the following list should be accepted as records of 86 cases of congenital porphyria, with 9 possible exceptions listed below:

Anderson,[22] 2, to which Mackey and Garrod [23] added the case of a sister; Arzt and Hausmann,[24] 2; Ashby,[25] 1; Barber,[26] 1; Baumstark,[27] 1; Schultz,[28] 1; van Berckel,[29] 1; van den Bergh,[30] 2, of which 1 was later studied by van den Bergh and Grotepass [31]; van den Bergh, Regniers and Müller,[32] 1; Bering,[33] 1; Böhm,[34] 1; Cant,[35] 1; Capelli,[36]

19. Kreibich, C.: Sklerodermieartige Lichtdermatose, Arch. f. Dermat. u. Syph. **144**:454, 1923.

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21. Rodelius, E., and Schumm, O.: Ueber Hämatoporphyrinogenausscheidung im Harn, Ztschr. f. urol. Chir. **3**:112, 1914.

22. Anderson, T. M.: Hydroa Aestivale in Two Brothers, Brit. J. Dermat. **10**:1, 1898.

23. Mackey, L., and Garrod, A. E.: On Congenital Porphyrinuria, Associated with Hydroa Aestivale and Pink Teeth, Quart. J. Med. **15**:319, 1922.

24. Arzt, L., and Hausmann, W.: Zur Kenntnis der Hydroa, Strahlentherapie **11**:444, 1920.

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26. Barber, H. W.: Two Cases of Hydroa Aestivale with Notes on Three Other Cases, Proc. Roy. Soc. Med. (Dermat. Sect.) **17**:18, 1924.

27. Baumstark, F.: Zwei pathologische Harnfarbstoffe, Arch. f. d. ges. Physiol. **9**:568, 1874.

28. Schultz, J. H.: Ein Fall von Pemphigus leprosus compliziert durch Lepra visceralis, Inaug. Dissert., Greifswald, F. W. Kunike, 1874.

29. van Berckel, G. J. J.: Porphyrien und Porphyrine: Eine Uebersicht und gleichzeitige Mitteilung von zwei neuen Fällen akuter idiopathischer Porphyrie, Geneesk. bl. u. klin. en lab. v. d. prant. **25**:1, 1928; abstr., Zentralbl. f. inn. Med. **49**:870 (Sept. 8) 1928.

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31. van den Bergh, A. A. H., and Grotepass, W.: Porphyrinämie ohne Porphyrinurie, Klin. Wchnschr. **12**:586 (April 15) 1933.

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(Footnotes continued on next page)

1; Cerutti,[37] 3; Dietzl,[38] 1; Ehrmann,[39] 3; Fraenkel, Hegler and Schumm,[40] 1; Freund [41] and Perutz,[42] 1; Gagey,[43] 2; Glaubersohn and Goldenberg,[44] 1; Gray,[45] 1; Greenbaum,[46] 1; Gottron and Ellinger,[47] 1; Gottron and associates,[48] 1; Günther,[5] 2; Herrmann,[49] 1; Jacoby,[50] 3; Kitagawa,[51] 1; Klee [52] and Schmidt-LaBaume,[53] 1; Kreibich,[19] 1;

33. Bering: Hydroa vesiculosa: Porphyrie, Zentralbl. f. Haut- u. Geschlechtskr. **48**:1595, 1934.

34. Böhm, A.: Hydroa aestivalis, Zentralbl. f. Haut- u. Geschlechtskr. **50**:359, 1935.

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36. Capelli, J.: Caso singular di hydroa vacciniforme con ematoporphyrinuria ed ipertricosi, Gior. ital. d. mal. ven. **55**:481, 1914.

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50. Jacoby: Hydroa vacciniforme, Zentralbl. f. Haut- u. Geschlechtskr. **27**: 472, 1928.

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Kren,[54] 3; Linser,[1] 1; Mackey and Garrod,[55] 1; Martenstein,[56] 1; Marcozzi,[57] 1; de Marval and Pons,[58] 1; Matsuoka,[59] 3; Meineri,[60] 1; Monocorps,[61] 2; Müller,[62] 2; Nebelthau [63] and Vollmer,[64] 1; Penner,[65] 1; Radaeli,[66] 3; Rasch,[67] 1; Rothman,[68] 1; Sato and Takahashi [69] and Toyama,[70] 3; Schreus and Carrié,[71] 2; Senear and Fink,[72] 1; Sparacio,[73] 1;

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71. Schreus, H. T., and Carrié, C.: Beobachtungen bei einem Fall von kongenitaler Porphyrie, Dermat. Ztschr. **62**:347, 1931.

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Stein,[74] 1; Strempel,[75] 1; Szilaghi,[76] 1; Taussig,[77] 1; Urbach [78] and Urbach and Blöch,[79] 2; Urbach [20] and Strasser and Urbach,[80] 2; Usuba,[81] 1; Vajda,[82] 1; Vamos,[83] 2; White,[84] 1, and Willbrand,[85] 1.

One patient of Ehrmann has been studied by Robitschek,[86] Gross,[87] Levitus [88] and Friede.[89] One patient of Günther's was Petry, already referred to. Günther said [6a] that Minkowski's case [90] was not a newly recorded one.

The 9 possible exceptions comprise the patient of Gottron and Ellinger,[47] the patient of van den Bergh, Regniers and Müller with coproporphyrin III in the urine, the patients of van den Bergh and of Monocorps without porphyrinuria but with porphyrinemia, and the 4 patients of Urbach and his co-workers, in whom the condition was atypical.

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72. Senear, F. E., and Fink, H. W.: Hydroa vacciniforme seu aestivale, Arch. Dermat. & Syph. **7**:145 (Feb.) 1923.

73. Sparacio, B.: Su un altro caso di hydroa acciniforme del Bazin, Arch. ital. di dermat., sif. **3**:239, 1928.

74. Stein, O.: Neue Befunde bei Hydroa vacciniforme, Zentralbl. f. Haut- u. Geschlechtskr. **25**:66, 1928.

75. Strempel: Hydroa vacciniformis (im Anschluss an Gasvergiftung?), Zentralbl. f. Haut- u. Geschlechtskr. **39**:23, 1931.

76. Szilaghi, S.: Hydroa vacciniforme, Zentralbl. f. Haut- u. Geschlechtskr. **40**:461, 1931.

77. Taussig, L. R.: Hypersensitivity of the Skin to Light, California & West. Med. **39**:301, 1933.

78. Urbach, E.: Hydroa vacciniforme mit Porphyrinurie, Lebertherapie, Lichtfilterprüfung, Zentralbl. f. Haut- u. Geschlechtskr. **44**:503, 1933.

79. Urbach, E., and Blöch, J.: Hydroa vacciniforme, Porphyrinopathie, Hepatopathie, Wien. klin. Wchnschr. **47**:527 (April 27) 1934.

80. Strasser, M., and Urbach, E.: Hydroa vacciniforme mit Porphyrinurie, Lebererkrankung und Klimacterium praecox, Wien. med. Wchnschr. **81**:1506 (Nov. 14) 1931.

81. Usuba: On Hydroa Vacciniforme, Jap. J. Dermat. & Urol. **28**:23, 1928; Zentralbl. f. Haut- u. Geschlechtskr. **30**:749, 1929.

82. Vajda, E.: Hydroa aestivalis, Zentralbl. f. Haut- u. Geschlechtskr. **50**:555, 1935.

83. Vamos, L.: Hydroa aestivale, Zentralbl. f. Haut- u. Geschlechtskr. **48**:518, 1934; **31**:784, 1930.

84. White, C. J.: Hydroa Aestivale (Acquired Adult Type), Arch. Dermat. & Syph. **29**:768 (May) 1934.

85. Willbrand: Hydroa vacciniformis, Zentralbl. f. Haut- u. Geschlechtskr. **41**:665, 1932.

86. Robitschek, W.: Ueber Haematoporphyria congenita, Ztschr. f. klin. Med. **101**:540, 1925.

87. Gross: Hydroa vacciniforme, Arch. f. Dermat. u. Syph. **105**:266, 1910.

88. Levitus, cited by Robitschek.[86]

89. Friede, R.: Ueber Hydroa vacciniformis des Auges, Klin. Monatsbl. f. Augenh. **67**:26, 1921.

90. Minkowski: Porphyrinuria, Med. Klin. **18**:194, 1922.

It is granted that there have been many other cases reported, some of which may perhaps belong to the list just given, falling into the "intermediate" category of Steglich,[91] to whose thesis the reader is referred. We have omitted reference to several interesting reports published during 1936.

INCIDENCE

Sex.—Of the 86 cases, the sex has been given in 82. Among these there have been 56 instances in men and 26 in women.

Age of Onset.—If the hypothesis of Mackey and Garrod[55a] may be accepted as true, that teeth stained red by uroporphyrin are an indication of porphyria beginning in early fetal life, the disease in 7 reported cases began then: those of Mackey and Garrod,[55a] Sato and Takahashi,[69] Meineri,[60] Kitagawa[51] and Marcozzi.[57] On those others on which pertinent data are available, the onset in 36 cases was in the first ten years, in 6 between the ages of 10 and 20, in 9 between 20 and 30, in 5 between 30 and 40, in 3 between 40 and 50, in 1 between 50 and 60 and in 1 between 60 and 70.

Familial Incidence.—Of the 86 cases, a familial incidence was recorded in 30, including 14 families. Of these, the condition was hereditary in 2. Possibly, had more attention been paid to the family in each reported case, the incidence would have been found to be considerably higher. At any rate, it was higher than that of nonporphyric hydroa, which Siemens[92] reported as 10 per cent.

Duration of Life.—Except in cases in which the condition is severest, life seems to be little endangered by porphyria. Deaths between the ages of 30 and 65 have been reported.

CLINICAL VARIATIONS OF PORPHYRIA

This study does not concern itself with cases of acute or probably acute porphyria. These will be studied in a later report. The material which follows concerns only the congenital disease.

Skin.—The most striking, and at the same time most common, phenomenon associated with porphyria is that of hydroa vacciniforme. It is, however, generally admitted that the manifestations of hydroa in the presence of porphyria differ considerably from those of hydroa without porphyria. The bullae are usually larger and do not show umbilication, and the recurrent attacks are accompanied with necrosis. Mutilations produced by the disease may become as extensive as in the mutilating form of lupus vulgaris, a feature which is never observed

91. Steglich, O.: Hydroa aestivale, Inaug. Dissert., Leipzig, 1932.

92. Siemens, H. W.: Studien über Vererbung von Hautkrankheiten, Arch. f. Dermat. u. Syph. **140**:314, 1922.

in cases of hydroa without porphyria, in which scarring is not nearly as extensive and the lesions not as numerous. A further difference can be seen in the duration of the two forms: While in the presence of porphyria the disease persists, as a rule, through life, hydroa without porphyria may cease spontaneously after puberty or later, as has been observed in a number of cases.

Hydroa vacciniforme is, however, not the only dermatosis associated with porphyria. As many as 14 cases of epidermolysis bullosa have been reported in this connection. Because of the frequent concomitance of the two dermatoses this has been overlooked for a long time, for even Jadassohn's *Handbuch* does not mention porphyria among the findings in epidermolysis bullosa. It must be said here that in some instances prophyrins have been found to be definitely absent, and in a case of severe congenital involvement in which examination was performed by one of us (W. J. T.) only minimal traces of coproporphyrin were found.

The reported cases are those of Ashby, Mackey and Garrod, Gray, Marcozzi, Meineri, Schreus and Carrié, Gottron and Ueberschär, Gottron and Ellinger, Sato and Takahashi, Taussig, Vamos, Urbach and Blöch and Cerutti. In 5 of these the patient had red teeth. In 4 cases hydroa predominated, but in 6 cases apparently epidermolysis alone was present.[93]

Scleroderma affecting other parts of the skin than those exposed to light was noted three times.[94] Calcification of the skin of the face was seen once.[75] Keloid formation was once a prominent feature in a white patient.[48a] Once firm subcutaneous nodules were reported.[44] Xeroderma pigmentosum was seen once at a site not usually exposed to light.[66a] The somewhat atypical condition in Monocorps' cases had been treated with gold preparations previously as lupus erythematosus. In 1 case hypertrichosis was the only dermatologic manifestation of the disease.[40]

Eyes.—In 9 cases there were ocular complications: conjunctivitis and chemosis in those of Vamos and of Radaeli,[66a] photophobia in that of Friede, bullae on the cornea in those of Jacoby, Senear and Fink and of Kuhnt, leukomas in those of Kuhnt and of Schmidt-LaBaume and posterior synechiae and symblepharon in those of Kren and of Willbrand.

Further details of the ocular manifestations of porphyria may be found in papers by Friede,[89] Levitus [88] and Kuhnt.[7]

Thyroid.—Toxic goiters were noted in 3 cases.[95]

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93. Cerutti.[37] Gottron and Ellinger.[48b] Schreus and Carrié.[71] Marcozzi.[57]
94. Rothman.[68] Müller.[62] Vollmer.[64]
95. Cant.[35] Taussig.[77] Müller.[62]

Liver.—Hepatomegaly was noted in 12 cases, all in men.[96] With this enlargement, disturbance of function has been observed several times.[45] Sometimes functional disturbance has occurred without palpable alteration of the liver. This disturbance of hepatic function has been assigned a place in the genesis of the disease by various authors, but the evidence for that assumption is scarcely impressive.

Spleen.—Splenomegaly has been found seventeen times. In cases in which the involvement is severe it apparently comes on earlier than in those in which it is mild. Unique was the case of de Marval and Pons,[58] in which there was hemolytic jaundice, which cleared up after splenectomy without influencing the porphyria.

Blood.—From data collected from the reported cases it can be stated safely that anemia constitutes a significant feature. Immediately striking is the presence of normoblasts and megaloblasts seen in 4 cases,[98] together with punctate basophilia and polychromasia. A study of the counts of Petry, whose early examinations showed a high color index and who was found at autopsy to have megaloblasts in his bone marrow and extramedullary erythropoiesis, furnishes an explanation for this and suggests that the same condition may have been active in a large number of patients who showed no evidence of primary anemia in the peripheral blood.

Regarding the anemia, some of the counts are instructive. With the persistence of porphyria, enough pyrroles are withdrawn from the stores in the body to rob the erythrocytes of their sources of hemoglobin. In spite of the formation of megaloblasts, which rarely gain access to the circulating blood, the color index diminishes as it does in any instance of severe secondary anemia. That not every patient becomes anemic is obviously due to the fact that the amount of porphyrin excreted varies enormously with the individual case. Further, it is certain that diet, under conditions of approximately equal loss of pyrrole, might determine whether anemia would be present.

Few chemical analyses of blood have been reported in this condition. Apparently the only patient in whom hematinemia has been observed was Petry. Both coproporphyrin and uroporphyrin have been repeatedly demonstrated in the serum, being found there in 3 cases in which none was demonstrable in the urine.[99]

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96. Borst and Königsdorffer.[8b] Schmidt-LaBaume.[53] Mackey and Garrod.[55a] Sparacio.[73] Capelli.[36] Radaeli.[66b] Sato and Takahashi.[69] Toyama.[70] Cerutti.[37b] Urbach.[20] Urbach and Blöch.[79]

97. Urbach.[20] Sato and Takahashi.[69] Robitschek.[86] Sparacio.[73] Gray.[45]

98. Ashby.[25] Gray.[45] Mackey and Garrod.[55a] Schmidt-LaBaume.[53]

99. Van den Bergh.[81] Monocorps.[61]

Content of Bullous Cutaneous Lesions.—Porphyrin was demonstrated once.[71]

Urine.—Although the urine in porphyria is described as red, the color may vary from pale pink to almost black. Further, often the urine when passed is a normal yellow and darkens only on exposure to light. This is due to the presence of porphyrinogen and urofuscinogen, which yield pigments on oxidation. During fever the urine has repeatedly been found to show normal with respect to pigment.[100]

The porphyrins found in the urine have been, in addition to those found in the urine of Petry, almost always uroporphyrin and coproporphyrin I. So far 2 cases have been found[101] in which there was excretion of coproporphyrin III but none of uroporphyrin III.

Feces.—The feces in porphyria are not characteristic unless their porphyrin content is high. Then they tend to be dark reddish brown when fresh, turning almost to black on oxidation.[6b] Coproporphyrin can be extracted after drying by Fischer's acetic acid-ether method.[102] Coproporphyrin and protoporphyrin are found in normal subjects but the amount of the former may be enormously increased in porphyria. Petry had about 0.1 Gm. daily. An excretion of 4.5 mg. per day has been reported.[51]

Pathologic Picture.—What little is known of the pathologic picture of porphyria is derived from biopsies of cutaneous lesions, extracted teeth and amputated fingers, from the study of capillary reactions and from three autopsies.

The histopathologic pictures of the skin in porphyric hydroa vacciniforme and in porphyric epidermolysis bullosa do not seem to differ from those in the nonporphyric forms of the diseases. In hydroa there seems to be agreement between all investigators as to the histopathologic observations; in their interpretation, however, some differences exist. The tendency seems to be to ascribe the necrotic epidermal and dermal changes primarily to capillary damage in the corium produced by light.[103] If this assumption is correct the condition dealt with is not a primary hypersensitivity of the epithelial cells, as has been suggested in regard to erythema solare and Hutchinson's summer prurigo, but a primary vascular change which in turn leads to necrosis of the corium and the epidermis.

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100. Arzt and Hausmann.[24] Fraenkel and others.[40] Gray.[45]

101. Van den Bergh and others.[32] Gottron and Ellinger.[48b]

102. Fischer, H.: Neuere Methoden der Isolierung und des Nachweises von Porphyrinen, in Abderhalden, E.: Handbuch der biologischen Arbeitsmethoden, Berlin, Urban & Schwarzenberg, 1926, vol. 1, pt. 2, p. 169.

103. Walters, M.: Hydroa vacciniforme, Dermat. Ztschr. **14**:263, 1907. Gray.[45] Schreus and Carrié.[71]

Examination of the teeth with ultraviolet rays [104] has demonstrated considerable deposition of porphyrin in the dentin with the calcium deposits, even though macroscopically they would not be considered to contain porphyrin. The teeth of a person with porphyria may vary from bright red to brown or yellowish or even look normal.

Autopsy Data: The essential data on Petry have been mentioned.[5] A proper appreciation of them can be obtained only by a study of the monograph of Borst and Königsdorffer. It should be noted, however, that in Petry's skin these observers found extremely fine granular deposits of porphyrin in the papillae immediately beneath the basal cells, demonstrable only by fluorescence microscopy.

There have been two other autopsies in cases of congenital porphyria: in that reported by Baumstark [27] and Schultz [28] and in that of Fraenkel, Hegler and Schumm.[40] The reports of these add nothing to what has already been said.

Sensitivity to Light.—The photosensitizing property of hematoporphyrin has been known for some time.[105] Since hematoporphyria was at first considered to be the porphyrin associated with porphyria, the etiologic connection between the two phenomena seemed established.[106] Later developments, however, have shown that the situation is actually far more complicated.

The experiments of Hausmann [2] and of Meyer-Betz [107] established beyond doubt that hematoporphyrin is capable of producing local and general sensitization to sunlight in animals as well as in human beings. Hematoporphyrin, however, is never found either physiologically or pathologically. Uroporphyrin and coproporphyrin are rather less active photosensitizing agents than hematoporphyrin,[108] but in any case, before their etiologic relation to hydroa can be considered proved, they must fulfil two minimum requirements: (1) the wavelengths causing hydroa

104. Maacke, C.: Die Histologie der Porphyriezähne, Vrtljschr. f. Zahnh. **47**:191, 1931. Fraenkel, E.: Experimentelles über Hämatoporphyrie, Virchows Arch. f. path. Anat. **248**:125, 1924. Mackey and Garrod.[55a]

105. (*a*) Raab, O., cited by Arzt, L., and Zieler, K.: Die Haut- und Geschlechtskrankheiten, Berlin, Urban & Schwarzenberg, 1935, vol. 2, p. 209. (*b*) von Tappeiner, H., and Jodlbauer, A.: Ueber die Wirkung der photodynamischen (fluorescierenden) Stoffe auf Photozoen und Enzyme, Deutsches Arch. f. klin. Med. **80**:427, 1904. (*c*) Hausmann.[2]

106. Günther.[5] Ashby.[25] Van den Bergh and Grotepass.[31]

107. Meyer-Betz, F.: Untersuchungen über die biologische (photodynamische) Wirkung des Hämatoporphyrins und anderer Derivate des Blut- und Gallenfarbstoffes, Deutsches Arch. f. klin. Med. **112**:476, 1913.

108. Kämmerer, H., and Weisbecker, H.: Ueber die sensibilisierende Wirkung der Porphyrine, Arch. f. exper. Path. u. Pharmakol. **111**:263, 1926. Fischer, H., and von Kemmitz, G. A.: Ueber die Einwirkung einiger Porphyrine auf Paramaecien, Ztschr. f. physiol. Chem. **96**:309, 1916.

must be the same as those causing reaction to light in porphyrin sensitization, and (2) the lesions of porphyrin sensitization must be the same as those produced in hydroa.

As to the former, there is no uniformity in the reported results on sensitivity to light in porphyric hydroa.[109] (The same, incidentally, is true of nonporphyric hydroa.[110]) In experimental animals the active wavelengths are in the region of 5,000 angstroms,[111] where both coproporphyrin and uroporphyrin absorb light strongly. It is surprising that most efforts to engender lesions experimentally on patients have failed, although there is little doubt that sunlight is actually the damaging agent.

Regarding the second requirement, it is evident that the lesions of hydroa are not the same as those produced in human beings by sensitization to porphyrin.[112] The latter is commonly described as an immediate erythema, followed at times by edema and, if the inflammatory reaction is more pronounced, by the formation of bullae.

There is considerable reason to believe, therefore, that sensitization to porphyrin may play little or no role in the production of the lesions of hydroa, but this point has not been sufficiently well studied to permit final judgment. It is imperative that care be taken in the future to differentiate between hypersensitivity of the skin and an altered reaction of the skin. Furthermore, the patient must be given that quantity of light which ordinarily produces the lesions before it can be said that light does not elicit the reaction.[113]

With respect to the role of trauma even less information is available. Positive Nikolski signs have been reported.[37b] In 2 cases a reaction could not be produced by light alone or by pressure alone, but bullae developed from the combination of exposure to light and trauma.[114] One patient was found to be sensitive to heat, pressure, pinching and friction [57] and another to both light and pressure.[71] One patient presented the clinical picture of epidermolysis bullosa yet reacted only to ultraviolet radiation.[60] An increased reaction to intracutaneous injection of histamine has been observed once.[62]

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109. Gottron and Ellinger.[47] Gottron and Ellinger.[48b] Freund.[41] Martenstein.[56] Gray.[45] Kitagawa.[51] Taussig.[77] Jacoby.[50] Schmidt-LaBaume.[53].

110. Epstein, S.: Experimentelle Eruption bei Hydroa vacciniformis durch Thorium X, Arch. f. Dermat. u. Syph. **168**:67, 1933.

111. Hausmann, W.: Ueber die sensibilisierende Wirkung des Hämatoporphyrins, Biochem. Ztschr. **30**:276, 1910.

112. Eidnow, A.: Photo-Dynamic Sensitization, Biological Action and Therapeutic Application, Brit. J. Dermat. **47**:277, 1935. Strauch, C. B.: Photosensitization, Am. J. Dis. Child. **40**:800 (Oct.) 1930. Meyer-Betz.[107].

113. Gottron and Ellinger.[48b] Epstein.[110]

114. Gottron and Ellinger.[47] Gottron and Ellinger.[48b]

Therapy.—Attempts at detoxification with metals (copper and zinc) have been made without success. The idea originated with the discovery in the feathers of an African bird of a substance called turacin, which proved to be the copper complex of uroporphyrin.[115] Calcium therapy has been tried without effect. Its use has been based on the diminution by calcium of the excretion of porphyrin in rabbit porphyria (lead).[116]

Recently, at the suggestion of Schreus,[117] liver therapy has been tried.[118] Reports of the results of this form of therapy have been conflicting,[119] and it seems to us that the place of liver in the therapy of porphyria is not yet defined. In view of the remarkable similarity of the bone marrow to that in pernicious anemia, it is desirable that this point be thoroughly investigated.

At present therapy of porphyria combined with sensitivity to light is limited to protection against light.[55b]

REPORT OF CASE [120]

Mrs. H. F., a woman aged 29, of Canadian and English-American parentage, came under our observation in the fall of 1934 and has been observed at irregular intervals. Twice, in 1934 and in 1936, she was hospitalized for study for a short period.

History.—The patient's maternal grandmother died of carcinoma of the breast and her father of "creeping paralysis" and arteriosclerosis at 57; her mother was living and well at 53. One brother, prematurely delivered, died in infancy. Of her 4 sisters, 3 are well and 1 has mild hyperthyroidism. All known relatives are blond. None have any condition similar to that of the patient. The living members of the family were not available for examination.

The patient had scarlet fever at 4 years. After this, she had repeated fainting spells, which persisted throughout her school years with diminishing frequency and recurred thrice during her first pregnancy. There had never been an aura, and there was never any evidence that she had had a convulsion.

The patient was married at 24; her husband was well. Her libido was normal. There had been two pregnancies, the first (two years after marriage) resulting in a daughter, who was well, and the second terminated by an induced abortion. Examination of the daughter's urine showed no abnormal amount or kind of porphyrin.

115. Fischer, H., and Hilger, J.: Zur Kenntnis der natürlichen Porphyrine: II. Ueber das Turacin, Ztschr. f. physiol. Chem. **128**:167, 1923.

116. Massa, M., and Battistini, G.: Porfirinuria sperimentale, porfirinuria patologica e loro scomparsa dopo introduzione endovenosa di sali di calcio, Pathologica **25**:28 (Jan. 15) 1933.

117. Schreus, H. T.: Ergebnisse und Probleme der Porphyrinforschung, Klin. Wchnschr. **13**:121 (Jan. 27) 1934.

118. Urbach and Strasser.[80] Urbach.[20]

119. Kren.[54] Müller.[62] Urbach.[20]

120. This case was presented by one of us (M. E. O.) at the meeting of the Chicago Dermatological Society on Dec. 18, 1935, with the diagnosis of "epidermolysis bullosa with hypertrichosis and melanosis" (Obermayer, M. E.: Arch. Dermat. & Syph. **33**:1091 [June] 1936).

Menstruation had started at the age of 13 and was irregular and painful until marriage. It had been regular since.

The patient's habits were normal, and she had nine hours' sleep per day.

Inquiry by systems showed no abnormality except for occasional headaches and transient swelling of the ankles. Her weight remained fairly constant between 135 and 140 pounds (61 and 63 Kg.).

Present Illness.—During childhood the patient had had attacks of blisters on the dorsa of the hands, which had been attributed to poison ivy.

Although originally she had reddish brown hair and a fairly light skin, since the age of 21 both hair and skin had gradually darkened, the hair turning almost black. At the age of 23 she first noticed that hair was growing heavily on her arms, legs and face. She learned how to use hot wax for depilation and had been doing this ever since without experiencing cutaneous reactions.

At about 20 years of age she noticed for the first time during the summer that blisters developed on the area where the strap of a golf bag rested on the shoulder. From that time on similar lesions appeared every summer when she carried a golf bag, but only on hot days. When she was 25, bullae developed on the hands, the elbows and the ankles after slight trauma, and this condition has recurred every year since, except during the months from November to April inclusive, during which the patient has always been free from lesions, with one exception. The bullae varied in size and depth. Some ruptured spontaneously, while the smaller, deeper-seated ones were opened by the patient "in order to relieve the pain." All the lesions left pigmentation, and those on the elbows and the ankles left atrophic scars. At one time the conjunctiva of the right eye became involved. This happened in the late fall. That same year the patient suffered from photophobia even when indoors during the winter; this was the only year when lesions developed on the fingers and the ankles during the cold season. Lesions appeared in spite of the fact that she had remained indoors for more than a week during a spell of exceedingly cold weather.

A further complaint registered was that of irritability. The patient evidently had periods during which she would fly into a rage with no provocation. These had diminished of late.

Physical Examination.—The patient's height was 167 cm., her weight 60.1 Kg. and her blood pressure 126 systolic and 82 diastolic with slight variations. The general appearance was that of a normally developed, well nourished, dark-skinned woman with hypertrichosis (fig. 2).

The color of the skin corresponded to that of a person of southern European extraction. The sites of normal pigmentation were accentuated; a brownish pigmented macule measuring about 2 cm. in diameter was noted below each axilla. There was no hyperpigmentation on the mucous membranes. The skin was moist and the temperature normal. The cutaneous lesions presented themselves at the first examination as vesicles and small bullae, arising from apparently normal skin, which on being opened contained a clear watery fluid. They were located on the backs of the hands. On the end phalanges of several fingers of both hands, milium-like lesions were present. There were ordinary abrasions on the hands, which, according to the history, had resulted from minor trauma, such as the pressure of a pencil in writing a note. In addition, numerous pigmented macules, varying in size and shape, were present, and for the most part symmetrically located, on the dorsa of the wrists and the hands, the forearms, the elbows, the ankles and the insteps. On the elbows and the ankles the lesions showed atrophy, with peripheral hyperpigmentation. On the sclera of the right eye a tortuous vesicular lesion 3 mm. in length could be seen; it was located midway between the cornea and the lateral angle of the eye, along the lower margin of the upper

lid. At a later date, the patient returned with a large bulla on the first finger of the left hand (fig. 3). On another occasion both conjunctivae were found to be slightly inflamed, and the patient had marked photophobia.

The hair was dark, almost black. There was definite hypertrichosis of the legs, the forearms, the chin, the cheeks and the forehead. The eyebrows were heavy

Fig. 2.—Patient with porphyria, showing melanosis and hypertrichosis of forehead.

Fig. 3.—Large blister resulting from friction during everyday work.

and the lashes long. Below the umbilicus there was a patch of long hairs. The distribution of pubic hair was feminine.

Examination showed no other abnormality. The liver and spleen were not palpable.

The Wassermann and the Kahn reactions of the blood were negative.

Examination of the blood showed 3,970,000 erythrocytes, 12.6 Gm. of hemoglobin (determined according to oxygen-combining power), 31.4 micromicrograms of mean copuscular hemoglobin (normal from 28.5 to 30.5), 5,000 leukocytes, 67 per cent polymorphonuclears, 26 per cent lymphocytes and 7 per cent mononuclears. One year later there were 4,340,000 erythrocytes, 85 per cent hemoglobin and 7,000 leukocytes.

Sternal puncture showed 45.6 per cent polymorphonuclears, 0.8 per cent eosinophils, 12.8 per cent lymphocytes, 5.2 per cent stab form polymorphonuclears, 8.8 per cent metamyelocytes, 9.8 per cent myelocytes, 0.2 per cent promyelocytes, 1.4 per cent myeloblasts, 16.8 per cent normoblasts, 0.4 per cent proerythroblasts and 0.2 per cent megalokaryocytes.

The values for blood sugar in the sugar tolerance test were: during fasting 67 mg., at one-half hour 125 mg., at two hours 122 mg. and at three hours 51 mg. per hundred cubic centimeters. (The normal values for the method employed range from 70 to 100 mg. during fasting.)

The basal metabolic rate was —10 per cent.

A urologic study with the view of ruling out an adrenal tumor resulted in normal cystoscopic findings, and a retrograde pyelogram showed a normal urinary tract.

A roentgenogram of the skull showed no abnormality.

Gynecologic examination showed a normal multiparous pelvis. Ophthalmologic examination revealed mild myopia; the visual fields were normal.

To determine whether ossification of the os multangulum majus was normal and whether there was thickening of the cortical portions of the long bones, roentgenograms were taken which revealed a normal right hand, left foot and left fibula and tibia.

Histologic examination of one of the cutaneous lesions on the dorsum of the hand showed the noncharacteristic features compatible with epidermolysis bullosa.

A diagnosis of epidermolysis bullosa with melanosis and hypertrichosis was made, and studies were undertaken concerning physical sensitivity and the presence of porphyria.

An attempt was made to reproduce the lesions experimentally. Heat was applied to the left shoulder for fifteen minutes. Below this the skin was rubbed briskly for a minute. Below this four areas of skin were exposed to the Kromayer lamp for intervals of ten, fifteen, twenty and twenty-five minutes, respectively. Three days later the patient returned; both she and a control gave negative reactions to all tests. Thereupon hard friction was applied for one minute to the shoulder, at the place where the lesions from the golf strap had been and to the right thigh. Intradermal injections of 0.1 cc. of serum from one of the bullae was made into the left thigh. There was no reaction of any note to any of these experiments.

While the patient was hospitalized for porphyria studies (February 1936) further attempts to elicit bullae were made. Since all gave negative results, only a brief description will be given of the method used.

As a source of ultraviolet radiation a "sunshine" or a "U" carbon was used, at 30 amperes and 15 cm. Radiation from these carbons is rich in ultraviolet rays and easily causes tanning. Over the patient's back was placed a cardboard screen with six holes. One of these contained no filter; the others held Corning glass filters nos. 338, 587, 986, 428 and 348. These permit a measure of isolation of various spectral regions from the ultraviolet through the infra-red. Exposures were made daily for ten minutes to the unfiltered spot and for from thirty to forty-five

minutes to the others. The exact superposition of the cardboard on its previous location was assured by marking the skin with 10 per cent solution of silver nitrate.

The only reaction was immediate erythema beneath the unfiltered spot and behind filters nos. 986 and 428. Since both of these pass only the nearer ultraviolet rays, a type of radiation not normally causing immediate erythema, this is notable, particularly since the absence of erythema behind the other filters rules out heat as a cause. Surprisingly minute vesicles formed beneath the silver nitrate, and the patient said they felt exactly like her former lesions.

Experiments were carried out to test the effect of changes in the vascular bed on the production of the lesions. Epinephrine was injected intracutaneously into one forearm and histamine tartrate into the other. One of us was used as a control. The reactions were normal, save that the patient's histamine wheal persisted for two days. On the day following the injections the forearms were exposed to unfiltered "U" carbon arcs for fifteen minutes. The only result was a subjective feeling of warmth at the site of the injection of histamine.

Tests with cantharides plasters showed no evidence of an increased tendency of the epidermis to peel. Further attempts to bring out an eruption by following friction with exposure to ultraviolet radiation were in vain, although in these attempts perhaps the friction was neither sufficiently intense nor prolonged.

Studies of capillary form and reaction were made by Dr. K. A. Reutherskiold. He reported that the capillary beds of the nails were normal in number, shape and action before and after injection of histamine hydrochloride (1:10,000), epinephrine hydrochloride (1:1,000) and acteylcholine hydrochloride (1:10) and scratch.

Studies with Porphyrin.—Studies with porphyrin were begun after it was found that the patient's urine was pink and contained much uroporphyrin which was soluble in ethyl acetate and amyl alcohol from the urine at p_H 3.2. The patient was hospitalized and put on a diet free from chlorophyll and hemoglobin. All urine and feces were collected. The studies were carried out by one of us (W. J. T.), with the following results:

Urine, collected for six days, contained at no time any urobilinogen, urobilin or bile pigments. Of particular interest was the absence of urofuscin.

For the isolation of the uroporphyrin the method of Waldenström [121] was employed, with a pure aluminum oxide powder as the adsorbent. The ammonium hydroxide eluate was acidified and extracted with ether to remove coproporphyrin (traces only), and the precipitate of uroporphyrin was esterified in methyl alcohol and sulfuric acid. It was taken into chloroform in the usual manner [102] and crystallized by precipitation with methyl alcohol. The crystals weighed 11.2 mg.; the porphyrin in the supernatant solution amounted to 28.7 mg. This method being practically quantitative, the patient excreted about 6.7 mg. of uroporphyrin per day.

This porphyrin was sent to Hans Fischer for identification. He reported that each fraction contained uroporphyrin I, the first with minute amounts of coproporphyrin. The second was carefully recrystallized by Dr. Libowitsky until the pure uro-ester was obtained, melting at 296 C., and showing no depression in melting point with Petry uro-ester. Thus it was established that our patient excreted uroporphyrin I.

Diet had no effect on her urinary excretion of porphyrin. The feces were dried and treated by Fischer's acetic acid-ether method and the extract examined for

121. Waldenström, J.: Untersuchungen über Harnfarbstoffe, hauptsächlich Porphyrine, mittels der chromatographischen Analyse, Deutsches Arch. f. klin. Med. **178**:38, 1935.

coproporphyrin.[102] While a large amount of copromesobiliviolin was found, there was only a minute quantity of coproporphyrin in 65 Gm. of dried feces.

The blood serum fluoresced bright green under ultraviolet radiation. Serum (10 cc.) was treated with acetic acid and ether and the extract examined with ultraviolet light rays. There was no evidence of porphyrin. The residue was treated with methyl alcohol saturated with hydrochloric acid gas, but no porphyrin could be found in the extract. By this method the presence of uroporphyrin was demonstrated (by W. J. T.) in the serum of a patient with acute porphyria at the Johns Hopkins Hospital.

Fig. 4.—Crystals of uroporphyrin-octa-methylester (× 250).

Ultraviolet microscopy of fresh blood smears showed no fluorescent erythrocytes. The serum contained neither hematin nor methemoglobin in a demonstrable amount.

Liver Diet.—After discharge from the hospital the patient was asked to eat heartily of liver. This she did, ingesting 25 pounds in twenty-three days. Seventeen days after beginning this she came in with a twenty-four hour specimen of urine containing approximately 8 mg. of uroporphyrin, more than she had excreted while on her hospital diet. At the same time she remarked that for the first time in her life she had had swelling of her ankles and eyelids before the menses. The ingestion of liver was stopped because the swelling spread to her left jaw and persisted. She later stated in a letter her hands burned like fire under any amount of pressure and that her menses were scanty.

The patient, who had always been fond of citrous fruits, now limited her diet almost exclusively to these on her own initiative and reported that she felt "really grand."

Sternal puncture was repeated, and the material obtained was forwarded to Professor Fischer at Munich, with the request that it be examined by ultraviolet microscopy. To date there has been no report on this.

SUMMARY

A definition of porphyria is given, and the chemistry of the porphyrins is elucidated. The present state of knowledge on this constitutional state is discussed. An evaluation of the original papers on the subject reveals 86 cases of undoubted "congenital" porphyria, the findings in which are analyzed. To these is added a new case, in which the condition was accompanied with epidermolysis bullosa, hypertrichosis and melanosis, and clinical and chemical studies are included. This patient excreted uroporphyrin I in the urine, with no metal complex or urofuscin.

The study of porphyria is still in its infancy. How to distinguish between a truly congenital error of metabolism and an acquired one secondary to some toxic agent is not yet known, nor is it known how to consider and treat certain conditions which show clinical aspects of both the "congenital" and the "acute" disease. The criteria employed for the recognition of porphyria are still vague, for no one can yet say how much porphyrin must be in the urine before a diagnosis of porphyria may be made.

Too few autopsies have been performed on patients with congenital porphyria for it to be known whether the picture presented by Petry warranted the sweeping conclusions drawn by Borst and Königsdorffer. Equally doubtful is the interrelationship between porphyria and such dermatologic entities as hydroa and epidermolysis bullosa.

We were unable to elicit the efflorescence typical of the condition in our patient, but our failure in this regard is one of a long series. The immediate erythema shown to rays from the near regions of the ultraviolet spectrum suggests both hypersensitivity and altered reactivity of the skin, and these are typical of porphyrin hypersensitivity in experimental animals. It is impossible to do more than guess at the nature of the protective mechanisms in man which prevent the more serious effects of porphyrin hypersensitivity produced by experimental injections.

We should like to put forward one hypothesis: In view of the existence of hydroa, epidermolysis bullosa and porphyria as independent clinical entities, and in consideration of the familial occurrence of each, it is suggested that each is a genetically different disease. The frequent

coexistence of porphyria and a cutaneous disease may depend on some spatial or chemical relationships of the genes determining these conditions.[122]

One word must be said about liver therapy. However enticing is the view in this regard, we have been unfavorably impressed with it. In view of the demonstration by one of us [123] that the fox squirrel has physiologic porphyria, it seems unlikely that there is actual hepatic disease in the genesis of human porphyria. Nevertheless it is to be hoped that further study of the disease, both in squirrels and in human beings, will shed more light on this problem.

CONCLUSIONS

1. It is suggested that porphyria constitutes a prenatal error of metabolism of pyrroles.

2. Patients with porphyria are protected against acute reactions to light by mechanisms which are yet undefined.

3. Hydroa and epidermolysis bullosa are thought to be genetically and etiologically unrelated to porphyria.

4. Although the therapeutic value of liver is doubted, further investigation of the subject is recommended.

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122. For a fuller explanation of the basis for this the reader is referred to Sir A. E. Garrod's "Inborn Errors of Metabolism," London, 1926.

123. Turner, W. J.: Studies on Porphyria: I. Observations on the Fox Squirrel, Sciurus Niger, J. Biol. Chem. **118**:519 (April) 1937.

TREATMENT OF ANGIOMA

BASED ON TEN YEARS' EXPERIENCE AT THE VANDERBILT CLINIC

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During the past ten years 408 cases of vascular nevi have come under observation at the Vanderbilt Clinic. Of these 319 were instances of hemangioma, including both strawberry marks and cavernous types, and 8 were cases of lymphangioma circumscriptum. Two hundred and two of the patients were 1 year of age or younger. There were 269 female and 139 male patients. Of the entire group, there were multiple lesions in 55 cases and single lesions in 353. In 253 cases the lesions were on the head, and in 211 they were on the face. The cheeks were involved in 57 cases (approximately 15 per cent) and the nose in 40 cases (approximately 10 per cent).

The discussion of treatment of hemangioma will be limited to the injection of sclerotic solutions, radium therapy, surgical excision and refrigeration with solid carbon dioxide.

SCLEROSING AGENTS

Treatment by the injection of sclerosing agents was given in 52 cases. Various solutions were used, including sodium salicylate, sodium morrhuate and a solution of quinine and ethyl carbamate (urethane). I have had decidedly the best results with quinine and ethyl carbamate.

Method.—Ordinary sterile precautions are observed. The area is first painted with tincture of iodine and alcohol. The only equipment necessary is a tuberculin syringe with a 25 gage hypodermic needle. This small needle enters the lesion easily, with the least possible tearing, resulting in minimal bleeding or loss of solution on withdrawal of the needle. The solution is preferably diluted with an equal volume of sterile water. Each cubic centimeter of the solution contains 0.1333 Gm. of quinine hypochloride and 0.0666 Gm. of ethyl carbamate before dilution. At first the amount injected into each lesion is no more than a few minims in any one area, the number of areas treated varying with the size of the lesion. Subsequently it is frequently advisable to use as much as 1 or 2 cc. of the half strength solution or smaller amounts of the full strength solution in one treatment of an angioma.

Each injection blanches a circular area extending about 8 mm. around the point of the needle. Injections into the vessels themselves are not necessary, because

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perivascular injections effectively thrombose the delicate structures. However, when the vessels are directly entered, the sclerotic action extends a little further, and the vessels, which were previously indistinguishable, are seen to whiten one after another. About the blanched area caused by each injection a margin of 5 mm. should be left untreated for the sake of safety. The injections should be placed sufficiently deep so that there will not be any necrosis of the overlying tissues, which would result in scarring. The object is to distribute small amounts of the sclerosing fluid through the deeper parts of the angioma. Thus, after introduction of the needle and injection of a minute amount, the needle is advanced a little and another small injection is made. Bleeding is slight and easily controlled by pressure for a few minutes after the injection. A dry dressing should then be applied.

The injections should not be made oftener than once a week. Sloughing and scarring are the major complications to be avoided. Sloughing may result from idiosyncrasy to the solution, overtreatment or too superficial injection. It is advisable to question adult patients regarding sensitivity to quinine. Because of similar possibilities in the case of infants, the first injection should be limited. I have experienced no serious difficulties from such sensitivity. In a few babies there has been a momentary reaction resembling the nitritoid reaction from arsphenamine. No treatment has ever been necessary, and the reaction has subsided in a moment or two. In some of the adults there has been tinnitus. A small injection in a ganglion of one adult was followed by sloughing of the skin that I suspect was due to idiosyncrasy, because it was unexplainable in any other way. I have never seen any important sloughing from injection into an angioma in a child. The temperature of infants may rise slightly after the injection, going up to 101 F. by rectum for a day or two. After the injection the lesion becomes somewhat swollen and tender, and this condition may last as long as two weeks, although it is greatest during the first three or four days. Some relief may be obtained by the application of cold compresses.

RADIUM

Radium therapy was used in 146 cases, either by external application or by interstitial implantation.

Method of External Application.—The external applicators were small trays or flat plaques. The trays contained tubes of radon or radium sulfate, so arranged in slots in a metal box that the radiation from them was evenly distributed over the surface of the applicator. Generally I employed flat trays containing emanation tubes, but I occasionally used flat plaques coated with radium sulfate. The filtration was with 0.5 mm. of silver or 2 mm. of brass or the equivalent, plus 2 mm. of rubber. Only brass filtration has been used during the past five years.

I have felt that the gamma rays emitted by these types of applicators are best suited for the desired selective effects on the radiosensitive, immature endothelium of the small blood vessels. This method of treatment has general approval.

For most lesions a distance of 1 cm. between the skin and the radium applicator was used. Distance therapy requires a larger amount of radium or longer exposure, but these disadvantages are fully offset by the benefits gained in producing an adequate dosage at the depth of the lesion, coincident with minimal absorption at the surface of the lesion. However, contact application was employed in lesions that were not over 2 or 3 mm. thick.

Shielding the normal skin about the angioma was accomplished by exposing the lesion through a hole cut in a sheet of lead at least 1/16 inch (0.16 cm.) thick. As many of the patients were infants, satisfactory shielding in protracted exposures was not always easy.

The dose is necessarily subject to many influences but is calculated to be about two thirds of an erythema dose. It is better to adhere persistently to an accepted standard than to experiment continually. The main injuries from radium therapy have been caused by excessive doses and experimentation by enthusiasts and novices. With this in mind, the operator should keep the dose low enough to avoid cutaneous reactions and bear in mind that radium therapy will not cure every angioma. The difficulties are lessened considerably if treatments are not given at intervals of less than three months. Such an interval seems sufficient to permit recovery from the effects of the treatment. The recovery is never complete but for practical purposes is sufficient to permit a repetition of the treatment until the total maximum safe dose has been reached. That there is a limit beyond which treatments cannot be repeated is well known. With the applicators and the doses recommended herein, this upper limit may be placed somewhat arbitrarily at six treatments to any one area. This figure does not mean that radium therapy should be persisted in up to a total of six treatments when there is no improvement from any of them. If there is no improvement after two, or at most three, treatments, some other form of therapy should be used. Four treatments was the average number required to cure a lesion in my series.

Gradual involution and disappearance of the lesion without cutaneous reaction is the aim. Clinical judgment of progress is of great importance. The lesion should be carefully watched between treatments, and the dose should not be repeated while any improvement is occurring or while there are other reactive changes in the normal skin or in the lesion. Such changes may be vascular irritability or epilation in the skin, and swelling, tenderness or active regression in the lesion. Hyperpigmentation is an individual factor of susceptibility that is of slight importance in estimating the therapeutic effect or dose. Desquamation, however, is a definite sign of overtreatment. For large angiomas it is a hazardous practice to treat multiple areas at the same time in order to expedite the cure. Only one area should be treated every three months.

For angiomas in infants the following doses for gamma ray trays are suggested:

Size of Applicator	Distance (Cm.)	Dose (Milligram hours)
Square, 2 by 2 cm. (4 sq. cm.)	1	200
Square, 4 by 4 cm. (16 sq. cm.)	1	350
Rectangle, 4 by 5 cm. (20 sq. cm.)	3	800
Rectangle, 2.5 by 1.7 cm. (4.2 sq. cm.)	1	250

When emanation trays are not available, flat, glazed salt applicators (plaques) may be substituted for them. The usefulness of either form of applicator depends entirely on its strength. The salt plaques should be at least of half strength and preferably of full strength (5 mg. per square centimeter), as weaker preparations consume too much time for accurate use with infants. Contact treatment with such plaques has been popular for cutaneous angiomas, and excellent results have been achieved by this technic. A glazed half strength plaque 2 by 2 cm. screened with 2 mm. of brass plus a rubber dam should be applied in close contact with the lesion for seven hours. Treatment should be repeated at intervals of three months, and not over a maximum of six treatments should be given to the same area of skin. There should be no increase in the dose or the frequency because

of lack of response. Contact applications may be made to large flat angiomas by dividing the tumor into areas slightly larger than the flat applicator and applying it with a brass filter to these areas, avoiding overlapping. When both the inner and the outer surfaces of the cheeks are involved, flat applicators applied to each surface may be arranged to cross fire. Long exposures may be divided into two or more periods, but the results are not the same or the dose as accurate as are those when the exposure is continuous.

Small lesions may be adequately irradiated with a brass tube applied at a distance of 2 mm. with a 2 mm. brass wall, distance being achieved by the thickness of a tongue depressor and the time of exposure for 25 mg. being two or three hours. Such a tube may be applied (in contact) to a small angioma on the lip for from thirty minutes to one hour, while the child is asleep.

Interstitial therapy by means of gold implants is used in the treatment of some bulky angiomas. It is particularly favored for those that are deep beneath the skin or for those that involve the mucous membranes of the lips, the tongue and other inaccessible parts. However, I usually prefer the injection of a solution of quinine and ethyl carbamate to the implantation of radium.

Method of Interstitial Implantation.—The gold implant, which contains radon, is a tiny gold tube approximately 4 mm. in length and 0.6 mm. in diameter with a wall thickness of 0.2 mm. This filtration absorbs most of the beta rays, so that, practically, only gamma radiation is emitted. For angiomas the implant should contain 0.8 to 1 millicurie, and such an implant should be used for each cubic centimeter. As these lesions are usually about 1 cc. in diameter, one implant is usually sufficient, but for larger lesions a greater number of implants is necessary, in which event due consideration must be given to the effects of cross firing. Because of the possibility of carrying infection deep into the healthy tissue, implants should not be inserted through an ulcerated surface, nor should they be used in badly infected growths, because the reaction to radium superimposed on the infection may lead to extensive sloughing that would not occur if the infection were not present. Frequently it is best to insert the implant by a puncture wound into the normal tissue beyond the edge of the angioma, push it interstitially to the center of the angioma and leave it there. It is important to insert the implant deep enough to avoid atrophy to the overlying skin. Great care should be exercised in placing the implant in exactly the best location in the angioma. It should lie with its long axis parallel to the surface but at a depth of at least 5 mm. from the surface.

The gold implants are sterilized by boiling and with strict asepsis are placed in trocars, there being one trocar for each implant. The trocar should be about 3 inches (7.5 cm.) long, which is sufficient for dermatologic work. The skin at the site of injection is painted with tincture of iodine and alcohol. If possible it is better to do without procaine hydrochloride, as some confusion may result from the swelling caused by its injection. While the operator is palpating and exerting courterpressure with the left thumb and index finger, the trocar containing the implant is introduced to the desired depth with the right hand. When palpation and inspection show that the end of the trocar is in the desired position, the implant is pushed out of the trocar by the stilet, and the trocar is slowly and carefully removed, counterpressure being exerted on the skin with the left index finger, so as not to pull the implant after the trocar. Bleeding is usually negligible. A small dry dressing may be applied.

After such treatment the angioma becomes swollen, especially during the second and the third week. After this time the swelling subsides completely, and the improvement is noticeable. It requires several months for the full benefits to appear.

REFRIGERATION

Refrigeration is an old method of treatment of established value. The modern cryocautery does not seem to have any advantages over the use of solid carbon dioxide, commercially known as dry ice. Because the treatment is simple and the improvement is rapid, refrigeration is particularly useful for small lesions on areas where cosmetic results are not of great importance. The treatment causes obliterative thrombosis of the vessels in the angioma and results in superficial necrosis that heals with a white, pliable scar, without any tendency, in my experience, to formation of a keloid.

SURGICAL PROCEDURES

Surgical excision was performed in 35 cases, mainly by Drs. John M. Wheeler, Jerome P. Webster and T. William Stevenson Jr. Excision with a scalpel is a good method of treatment for small angiomas situated on the upper eyelid and is useful for other angiomas situated near the eye, on the scalp or on the extremities and those that for one reason or another are not to be treated by injection or irradiation. Surgical removal is accompanied by surprisingly little bleeding, as most of the lesions contain a good deal of connective tissue. Grafts when necessary about the eyes are made from the other lid or from skin of the postauricular region, though it is often possible to close the wound by sliding over it a piece of skin from the same eyelid. The panniculus of an infant, compared with that of an adult, is proportionately so much larger than the frame that it is possible to make excisions of sizable lesions in infants with results far superior to those obtainable in adults. Recurrences after surgical removal are rare.

COMPARATIVE RESULTS

Of the 146 cases in which treatment with radium was completed, in 18 there was ulceration or scarring as a result of trauma, infection or treatment with solid carbon dioxide before the patient came under my care. Of the remaining 128 cases, in 95 I obtained a perfect result with no atrophy or scarring. In other words, one could not determine the site of the angioma in 75 per cent after treatment. There was an additional group of 33 cases in which the end-result, though not perfect, was satisfactory to both the parents and myself. In 22 cases of this group there was either a slight bulging of the skin or a faint persistent redness, due to a remnant of the angioma. In the remaining 11 cases

atrophy occurred. In 9 of these treatment with filtration through 0.5 mm. of silver was given in 1927 and 1928. In 7 cases the atrophy was scarcely perceptible and not at all objectionable. There was only 1 case in which atrophy followed treatment with brass filtration and the technic which my associates and I have been using since 1929. In 4 cases (2.7 per cent) there was objectionable atrophic scarring with telangiectases. In 3 of these treatment with silver filtration was used in 1928, and in the other gold implants were employed in 1930. There was an arrest in bony development in 1 case, and cataract developed in another. Both of these were cases in which silver filtration had been used in 1928 for extensive angioma of the face. However, I do not believe that any better results would have been accomplished with brass filtration in either of these cases. Today I should treat the lesions with injections of quinine and ethyl carbamate. It has been customary in all cases in which treatment with radium was used to keep the patient under observation for at least five years after the completion of treatment, and many of the cases reported on herein have been observed for nearly ten years.

The results accomplished with radium may be compared with those by other methods of treatment. In all the cases in which treatment by surgical excision or refrigeration was used there was naturally slight scarring, but the cosmetic results, especially from surgical measures, were splendid. These methods have a field of usefulness in the treatment of some lesions of favorable size and situation.

Kelly and I [1] were among the first to use injections of sclerosing solutions in the treatment of angiomas. Since the time of our report I have learned much about the value of this method by observing the results obtained by Dr. George U. Carneal from the injection treatment of angiomas in the clinic for the treatment of varicose veins. After six years' experience with this method my associates and I have found that its effectiveness equals that of radium therapy; that, aside from the possibility of hypersensitivity to quinine, it possesses no hazards, and that the duration of treatment is shortened appreciably by it. I state without hesitation that it is a good method of treatment and to a great extent will take the place of radium therapy. Perfect results were obtained in 70 per cent of the cases in which the angioma was treated by the injection of a sclerosing solution. In 10 per cent only a small remnant of the angioma was present at the cessation of treatment, and this was not sufficient to be objectionable. Slight and scarcely visible scarring occurred in 12 per cent of the cases in which such treatment was employed. Small depressed scars and keloidal scars each occurred in 4 per cent of the cases.

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1. Andrews, G. C., and Kelly, R. J.: Treatment of Vascular Nevi by Injection of Sclerosing Solutions, Arch. Dermat. & Syph. **26**:92-94 (July) 1932.

Fig. 1.—Hemangioma before (*A*) and after (*B*) five treatments with a gamma ray tray, at a distance of 1 cm., about 35 milligram hours being given per square centimeter, with intervals of three months between treatments.

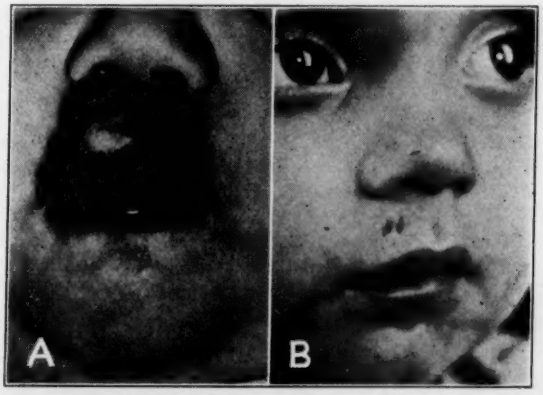

Fig. 2.—Hemangioma before (*A*) and after (*B*) twenty injections of full strength solution of quinine and ethyl carbamate (2 to 15 minims) into the center of the mass through the mucous membrane and subcutaneously. The intervals between injections varied from one week to two months, for a year. (These photographs were supplied by Dr. George U. Carneal.)

Although in general the results achieved with injection were as good as those following radium therapy, there were a few instances in which such spectacular results have been obtained on extremely radiosensitive hemangiomas with two or three small doses of radium that I do not say that treatment by injection should entirely displace that with radium. The problem of dermatologists is to determine which hemangiomas possess an extreme degree of radiosensitivity. My records and various experiences offer little on this point except an impression that hemangiomas that are extremely radiosensitive are bright red, being either of the strawberry mark or of the cavernous type, such as shown in figure 1 *A*. In the treatment of lymphangioma circumscriptum, the results of injection of sclerotic solutions were better than those of radium therapy.

CONCLUSIONS

1. There are marked individual variations in the radiosensitivity of hemangiomas.

2. Treatment with radium should be limited to angiomas which are particularly radiosensitive and should not be used near the eye or on extensive lesions over bony prominences.

3. Gamma radiation obtained by filtration through 2 mm. of brass or its equivalent gives better results than softer radiation. Except for superficial lesions, a distance of 1 cm. or more between the radium applicator and the skin is desirable.

4. Injection with a solution of quinine and ethyl carbamate is the best treatment for hemangiomas about the eyes and on the lips and for extensive lesions on the sides of the face or on the hands and the wrists. It is usually the best treatment for relatively radioresistant hemangiomas, whatever their locations may be, and for lymphangioma circumscriptum. Treatment by injection should be employed more extensively than it is at present because of its effectiveness, freedom from danger and simplicity.

ABSTRACT OF DISCUSSION

Dr. E. Lawrence Oliver, Boston: I wish to congratulate Dr. Andrews on the excellent results he obtained. I should like to call attention to the fact that many lesions of the cavernous type will disappear spontaneously. It may take many years, but when they do disappear spontaneously I believe the result is better than that obtained from any form of treatment.

Dr. S. E. Sweitzer, Minneapolis: Dr. Oliver mentioned the fact that many of these angiomas disappear spontaneously. I observed a case in which the son of a banker had an angioma on the side of the leg, and when I told him it might disappear spontaneously he decided not to have it treated. I have seen the young man recently, and there is now only a slight scar.

In regard to medication, Dr. Andrews may some day meet a sensitive patient and have trouble. If the solution used for the treatment of varicose veins is

spilled outside the vein, it causes sloughing. I think great care should be used in injecting any solution. For many years, instead of either quinine and ethyl carbamate or sodium morrhuate, to which a number of persons are sensitized, I have used alcohol. There is no bother about getting into a vein, for alcohol can be injected wherever desired. The results are as good as those with the other agents, and so far I have found no one who is particularly sensitive to alcohol; so it can be used with safety.

In connection with radium therapy, I have for some time been using roentgen therapy. When radium is used, a large amount is necessary, and it must be highly filtered. At the University of Minnesota my associates and I use filtered roentgen rays, and the only difficulty we have is that when one is treating an infant it is necessary to anesthetize him with chloral hydrate in order to keep him still. We use 600 roentgens and repeat the dose when shrinking of the lesion stops. So far, we have had no bad results and just as good results as we obtained with radium.

Dr. H. J. Parkhurst, Toledo, Ohio: In the treatment of cavernous hemangioma for several years I used a 10 mg. radium plaque in almost all cases. My observation was that frequently so much treatment was required that there was considerable danger of unfavorable sequelae. Therefore, I used electrodesiccation and found the results satisfactory. However, when the extreme rarity of these hemangiomas in adults is considered, it seems likely that they do tend to disappear spontaneously. For this reason I usually advise the parents to take the child home, wait a while and get in touch with me later if they feel that the lesion is enlarging.

Dr. Paul E. Bechet, New York: I have always been interested in the spontaneous disappearance of angiomas. My attention was first called to this subject many years ago, when I observed a large cavernous angioma on a child about 8 months of age. The lesion was about 8 mm. in diameter, involved the entire right eye and extended to the hair line. The lesion was so large that the eye was completely closed, with resulting purulent infection. There were one or two small ulcerated lesions on the angioma. I advised washing the eye with boric acid and applying boric acid ointment to the ulcerated lesions. The child did not return for further observation. Five years later the patient came to the office for the relief of scabies. Over the site of the old angioma, which had entirely disappeared, was a smooth pliable scar, and there was no deformity of the eyelids. Thinking that this remarkable result had been obtained through treatment, I ascertained, to my surprise, that the child had not seen a physician and that the parents ascribed the excellence of the result to boric acid ointment. That angiomas are rather common in early childhood and are rarely observed in adult life can, in all probability, be ascribed to spontaneous disappearance rather than to treatment. In my opinion, spontaneous disappearance is much more common after traumatism of the lesion. I think Dr. Parkhurst has been wise in stressing the occasional poor cosmetic results of radium therapy. The process is slow, and even when the treatment is given with unusual skill it occasionally results in marked atrophy and telangiectasia. If another method can be elaborated which will give equally good results and with which there will be less chance of a poor cosmetic result, that method should be favored.

Dr. J. H. Swartz, Boston: I believe that if obstetricians and pediatricians were taught to refer a child to a dermatologist for treatment of a vascular nevus as soon as it is noticed, while the lesion is still small, a good many extensive lesions requiring medical therapy could be avoided.

Electrodesiccation of a pea-sized angioma is simple and effective. I do agree that nature takes care of some angiomas, but at present there is no way of telling which ones will disappear without treatment.

Dr. Eugene F. Traub, New York: Several years ago I asked the members to answer a questionnaire as to what types of vascular nevi they had personally seen disappear spontaneously. The results were of considerable interest, because many members had never actually seen vascular nevi disappear. Others insisted that the majority disappear if left alone. One reason stated for this belief was that they were so rarely seen in adult life. Since then I have kept close watch in all my own cases, and I believe many nevi do disappear without treatment. In some instances this disappearance is incomplete—sometimes trauma or ulceration occasions the regression—but some nevi do disappear without a trace and without ulceration, leaving skin of absolutely normal texture. It is not advisable because of this to sit back in all cases, however, and await this spontaneous disappearance. Watchful waiting should be pursued only in those cases in which the lesion at the time of the first observation is stationary or has already begun to regress. If the lesion is enlarging when first seen, treatment should immediately be instituted, because the earlier this is done the better is the final cosmetic result, with the least amount of treatment. I find that now when employing radium I never give treatments closer together than at intervals of from four to six months, and often it is not necessary to give more than from one to three such treatments. For cavernous nevi I now prefer treatment by injection to radium therapy, because I believe the procedure is much easier to carry out, because any possible sequelae of radium therapy are avoided, and because such treatment often is much more efficacious. I believe that often all that is necessary is to arrest the growth and that the lesion, once it has begun to disappear, will naturally continue to regress. If the regression occurs without ulceration, the end-result is superior often to that of any treatment that may be instituted; but if the disappearance follows ulceration, as it does, perhaps, in the majority of cases, then the end-result is not as good as could have been achieved had treatment been instituted early.

Dr. George C. Andrews, New York: Answering Dr. Sweitzer in regard to ulceration in cases of varicose veins, I should say that the treatment for that condition is not exactly comparable to that of angioma, for in cases of varicose veins the vessels are relatively superficial, while in cases of angioma they are deep, and small amounts of medication may be distributed in the depths of the lesion. Enough injections have been given since 1932 to afford an opportunity to encounter bad results if they are in store. I consider this method in some cases superior to radium therapy, and it does not possess any of the hazards of that agent.

ECZEMATOUS ERUPTIONS PRODUCED BY LEAVES OF TREES AND BUSHES

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Many eczema-producing substances, such as ethereal oils, resins, balsams, organic acids and alkaloids, are of vegetable origin. It is well known that eczema may be caused by plants, even though the active substances have been isolated and chemically analyzed in only a few instances (Bloch's primin in Primula obconica) or demonstrated in some other way, as a rule by patch tests with substances known to be present (limonene and citric acid in lemon eczema and pinene and abietic acid in pine eczema). The active elements are most often leaves, petals and fruits, less frequently roots or bulbs, as a rule from annual herbaceous plants, wild and cultivated (flowers, vegetables and utility plants).

Among the ligneous plants (bushes and trees) particular attention has been paid to the wood and the bark. Many "exotic" trees are known to produce eczema through contact with the wood, but some trees that grow in a temperate climate are also known to produce this effect through their wood (pine, oak and alder). With the exception of Rhus toxicodendron (poison ivy), however, this ability to cause eczema has been demonstrated infrequently in the leaves of such plants, although the evergreen and more or less leathery foliage of box, ivy, dwarf medlar, witch-hazel (Hamamelis virginiana), Port Orford cedar (Chamaecyparis lawsoniana), Chinese arbor-vitae (Thuja orientalis), fig, myrtle and eucalyptus has been mentioned.[1] Of deciduous trees we have found only one mentioned in the literature: hop-hornbeam (Ostrya virginiana), a sort of ironwood belonging to the birch family.[2]

Thus, the leaves of herbaceous plants and the wood of trees appear to be well known as possible causes of eczema, but it is our impression

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From the Department of Dermatology, Finsen Medical Light Institute.

1. For list of references to the literature, see Touton, K.: Hauterkrankungen durch phanerogamische Pflanzen und ihre Produkte, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1934, vol. 4, pt. 2, p. 486. Weber, L.: External Causes of Dermatitis, Arch. Dermat. & Syph. **35**: 129 (Jan.) 1937.

2. White, James C.: Dermatitis Venenata: A Supplement List, J. Cutan. Dis. **21**:449, 1903.

that the possibility of an eczematous eruption due to the leaves of trees and bushes is seldom considered and rarely investigated by patch tests. We have had occasion to diagnose eczema of such origin in several instances, the cutaneous eruption being produced by the leaves of eucalyptus, myrtle, prune, alder, elm and magnolia, only the first of which appears to have been mentioned in this connection before.[3]

In this paper two cases of eruption due to elm leaves are reported, together with one case of occupational eczema caused by magnolia leaves.

REPORT OF CASES

CASE 1.—On Oct. 24, 1935, a watchman aged 35 applied to the clinic for treatment of eczema of the fingers that had persisted for several months. The history of his illness was as follows:

Three years previously (August 1932) the patient had had acute eczema of the face, with redness and moisture. At that time he was laying tracks for a railroad. He handled the carbolineum-saturated railroad ties and in strong sunlight was often exposed to the fumes from these ties. The eruption was treated with a powder, and it subsided in two weeks. Apparently no effort was made at that time to ascertain the cause of the eruption. There was no relapse during the following winter.

During the next spring the eruption reappeared in the same acute manner and was localized on the face. The patient had quit his previous work and was now a night watchman in the army laboratory on the old Christianshavns rampart. He applied to another dermatologic clinic, where the eruption was interpreted as solar dermatitis and treated with calamine lotion. His work as a night watchman consisted of indoor and outdoor inspection, and in addition he tended the heating plant in the evening and fired small furnaces in the laboratory with coal and coke. Thus his face and hands were exposed to heat from the fires. He noticed that this heat caused some irritation of the eruption but thought it could hardly have had any primary noxious effect, as the firing caused no eczema in the winter. The facial eruption persisted throughout the summer and autumn but varied somewhat in intensity. During the following winter he was again free from any eruption.

In the spring of 1934 there was again an acute eczematous eruption on the face, lasting all summer and disappearing in the autumn. He received the same treatment as before, as the condition was still considered to be solar dermatitis.

In the spring of 1935 the eczema reappeared, localized on the face as a vesicular eruption and accompanied with redness and edema, especially around the eyes. He applied again to the same clinic, where the diagnosis of "solar eczema" was still maintained.

Shortly after the appearance of the facial eczema he noted for the first time a limited vesicular eczema on the second finger of the right hand. As before, the facial eruption again subsided late in the autumn. The digital eczema persisted, however, and on this account he applied to the dispensary of the Finsen Medical Light Institute. In spite of various forms of treatment, the eczema spread during the following weeks to other fingers, but the face remained free. By the latter part of January 1936, however, it had practically disappeared, even though

3. Galewsky: Ueber Eucalyptus-Dermatitiden, Dermat. Ztschr. **12**:36, 1905.

a few abortive vesicles appeared now and then in the following months. These yielded to treatment with a zinc paste.

In the middle of May 1936 the patient returned, presenting an acute recurrence of the facial eczema (fig. 1), accompanied with exacerbation of the digital eczema. Except for the affected areas, the skin was normal—neither particularly dry nor oily—and there was no scaliness of the scalp.

A suspicion now arose that there was some injurious agent other than sunlight —in particular some plant—because of the striking seasonal recurrence. As night watchman the patient had to walk a great deal on the rampart of Christianshavn, and this fact suggested the possibility of contact with leaves of toxic action He had been examined previously with the series of eczema tests generally employed in this institute,[4] but all tests had given negative results.

Fig. 1 (case 1).—Eczema due to elm leaves.

He was then asked to bring leaves of all the wild herbs, bushes and trees growing on the rampart. Two days later he returned with leaves of dead-nettle, hemlock, hawthorn, brier, dandelion, elder and elm. Patch tests with these leaves showed a positive reaction for elm but negative results for all the others. A supplementary test was made with the wood of elm, and this produced no reaction.

When the patient was told about the possible connection between elm leaves and his eczema, he stated that there were a great many shrubby elms growing wild on the rampart and that he was often hit in the face by leaves and branches

4. Tests with primula, pinene, rosin, solution of formaldehyde, paraphenylenediamine, paramidophenol, chromate, nickel, mercury, silver, quinine, iodine, peruvian balsam, coal tar, pine tar, pyrogallol, resorcinols, salicylic acid, chrysarobin, a perborate washing powder and potassium soap.

of these elms. He recollected too that during the first year of his trouble with this condition, while working on the railroad, he would pass through a small grove of elm trees on his way to work. The probability that the elm leaves were the cause of his eczema was further strengthened by the fact that on repetition of the patch test with these leaves there was a slight exacerbation of the cutaneous lesions on the face as well as on the hands.

In 1936 too the eruption subsided late in the fall. In the past it had been complicated by the presence of several furuncles, at first on the fingers and later on other parts of the body. As already mentioned, the intensity of the cutaneous condition was greatest when it first appeared, i. e., in the spring. It then varied and on the whole was less pronounced in the latter part of the summer. It is possible that this gradual amelioration was connected with a partial and gradual desensitization, which was lost in the winter when the patient did not come in contact with the leaves in question; or perhaps this phenomenon may have been due, to some extent, to a greater toxicity of leaves in the spring, when they are fresh and green, than later in the summer, when they have been dried somewhat by the sun and the wind.

Control patch tests were made on 67 subjects. Among these, a negative reaction appeared in 50 and in 17 (about 25 per cent) a positive reaction. This was a really surprising number. As a rule, the positive reaction occurred within forty-eight hours, with some individual variation of intensity, appearing in some instances as mere redness, while in others it presented scattered papular elements (vesicopapules) or slight infiltration. Perhaps this was a matter not of sensitization but of toxicodermatitis in the pharmacologic sense. Further investigation of this point had to be postponed, as the season was too far advanced for collecting the leaves for preparation of the extracts.

In the future, no doubt, attention will have to be paid to elm leaves as an eczema-producing factor, on account of both the frequent reactions demonstrated in our control material and the common occurrence of this tree in countries with a climate similar to that of Denmark. The elm is widely employed not only as a shade tree but as a shrub for hedges and arbors. The two species most common in Denmark are Ulmus campestris (small leaves) and Ulmus montana (large leaves). The leaves of the former are more hairy than those of the latter. Patch tests were made with the upper as well as the lower surfaces of the leaves, apparently without any essential difference in the reaction.

This case is of further interest because it shows that when spring and summer eczema is localized on parts of the skin exposed to sun and light the possibility of other injurious factors besides light has to be kept in mind. For that matter, the patient stated that he often took sun baths in the open, both in spring and in summer, without any ill effects. Furthermore, he thought he had noticed an exacerbation of the eczema after sitting in an arbor of lime-trees (elms?).

Case 2.—The patient was an agent, who applied to the dispensary on July 21, 1936. His past history showed no disease of the skin.

He presented a vesicular eczema of three weeks' duration, which occupied the backs of both hands and extended up both forearms, chiefly as scattered or confluent patches of erythema, forming a vesicle here and there. On being questioned the patient stated that shortly before the appearance of this lesion he had trimmed a rowan hedge and at about the same time a hedge of elms. He was inclined to associate the eczema with the first of these two factors—that is, if there were any conceivable connection between his cutaneous condition and the trimming of a hedge. No information could be obtained about other external eczema-producing factors,

for the patient was an agent and claimed that he was never in contact with any irritating chemicals.

To throw light on the cause of the eczema a trichophytin test, ordinary patch tests for eczema and patch tests with rowan and elm (Ulmus montana) leaves were made. The results of all except those with elm leaves were negative. On further questioning it was found that the patient had never trimmed an elm hedge before. The hedge in question belonged to a friend. When told about the presumable connection between the elm leaves and the eczema, he recalled that another friend who lived in the same house had had a similar eruption after trimming the same hedge, except that the eczema of his friend had an almost universal extension.

The eruption was treated with a soothing lotion and subsided in a short time. There has been no relapse at the time of this report.

Case 3.—The patient was a dyer, aged 22, who came under observation on Nov. 5, 1936. About one month before, for the first time, an acute pruritic vesicular eczema had appeared on the backs of both hands. At that time he was occupied in boiling magnolia leaves in a pot containing a solution of red aniline dye, the vapors arising from the pot coming in contact particularly with the skin of the hands. The condition subsided largely in two weeks. Ten days before examination, when he again was occupied with the same work, there was a relapse of the eruption, this time on the face, as the hands were protected with rubber gloves. The facial eruption was moist and crusted. When he stopped this work, there was again a distinct improvement, but three days before the examination the lesion was again aggravated. This time the patient had not been occupied with the previously mentioned work. Several times he passed through the room where the boiling process was carried on and noticed that vapors caused an exacerbation of his condition. Merely passing by the open doors of this room, he thought, made the eruption worse.

The magnolia leaves used for this purpose were of the species Magnolia grandiflora, which does not grow outdoors in Denmark. Fresh green leaves are imported from Italy and Switzerland and are treated by boiling 1 or 2 Kg. at a time in a solution of red aniline dye in large vessels. This dyeing of magnolia leaves takes place only in October and November, whereas leaves of other plants are dyed all year round with the same or chemically related aniline dyes. Work with other kinds of leaves had never caused him any inconvenience.

On examination the patient presented an acute eczema of the backs of both hands and the adjacent parts of the forearms. The lesion consisted of small discrete or grouped vesicles, crusts and slight pigmentation. Similar changes were seen on the face and the ears, and there was edema around the eyes.

From the time of its occurrence it was obvious that the eruption was associated with the aforementioned work. Further, it seemed most likely that it was attributable to the magnolia leaves and not to any other kind of leaves or to the chemicals employed in dyeing. For the sake of certainty, however, patch tests were performed with the aniline dyes employed in that shop—rhodamin, cerise, diamond green and chrysoidin. All gave negative results. Patch tests made with both green and prepared leaves of magnolia grandiflora gave positive results. The positive reaction appeared as a mere marginal (vesicular) reaction corresponding to the margin of the square piece of leaf applied to the skin. This phenomenon seemed attributable to the fact that the leaf was thick, so that the juice came in contact with the skin only at the margins of the patch. The proof of this was furnished when a new piece of leaf was perforated with a pin in several places prior to its application to the skin. After forty-eight hours there was a uniform vesicular reaction. The upper surface of this sort of leaf is an ordinary green, while the

lower surface is nearly chocolate colored. Both sides of the leaf were used in the test, and both produced the same positive reaction. Control tests on 50 other patients with eczema gave negative results.

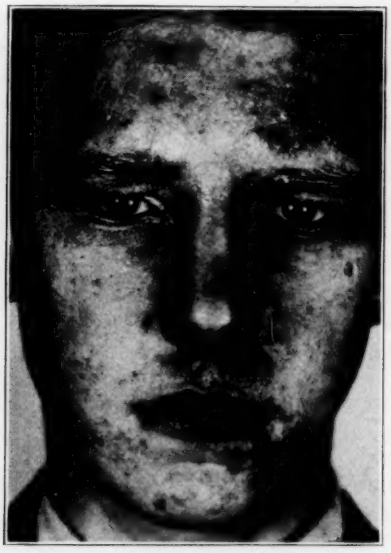

Fig. 2 (case 3).—Eczema due to magnolia leaves.

Fig. 3 (case 3).—Eczema due to magnolia leaves.

As already mentioned, the species of magnolia dealt with (Magnolia grandiflora) does not grow in the open in Denmark but is cultivated in hothouses, where the leaves are much thinner and not colored on the lower surface. A patch test was performed with such a leaf, obtained from the Botanical Gardens, and there was a positive, uniform, vesicular reaction.

Although the season was far advanced (November), we succeeded in obtaining a leaf of a species of magnolia (Magnolia hypoleuca) which grows in the open in this country. A patch test with this leaf also gave positive results, but the reaction consisted of only a few scattered papules. It may be, however, that the weaker reaction was due to the fact that the leaves were somewhat dried and a little damaged by the harsh autumn weather.

The present data leave no doubt that the eczema in this patient was produced through a specific sensitization by the vaporizing juice of the magnolia leaves and that this hypersensitiveness may be produced by several (perhaps all) species of the magnolia family.

As to the frequency of hypersensitiveness to the leaves of this plant, nothing definite can as yet be said. The plant has not been mentioned in the literature before as a producer of eczema, but it will now be reasonable to consider it a possible cause in countries with a warmer climate, where the plant is more common and grows outdoors.

SUMMARY

It is pointed out that while eczema is known to be produced by the wood of many different trees, only slight attention has been paid so far to the leaves of trees (and bushes) as possible producers of eczema, though the causative role of the leaves is well known in many herbaceous plants.

To illustrate this point, three cases of eczema are reported, in two of which the condition was produced by leaves of elm and in one by magnolia leaves. The eczema-producing effect of the leaves of these trees has not been previously mentioned in the literature. In all three cases the diagnosis was verified by patch tests.

NOTE.—A few months after the report of the aforementioned case was submitted a similar case came under observation at the clinic. The patient was a young girl engaged in the same kind of work as that of the patient in case 3, for the same firm, and she suffered from eczema of the hands. After her contact with magnolia leaves was discontinued, the eruption yielded to treatment fairly rapidly. This patient stated that several fellow employees had had similar eruptions (on the hands and the face) during October and November, when the special preparation of the magnolia leaves took place. In these cases, however, the eruption was more transitory and disappeared rapidly when the work was discontinued. These data suggest that the magnolia leaves here concerned possess a great power of sensitization.

The magnolia leaves are used for wreaths and other herbal ornaments.

LEUKOPLAKIA BUCCALIS

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This study is based on three hundred and twenty-seven cases of luekoplakia among 16,802 veterans (1.9 per cent) examined at the Veterans Administration Facility at Washington, D. C. The group examined was made up almost exclusively of men, and less than 5 per cent of them were Negroes. Almost all the men examined were World War veterans, so that the average age was about 40.

A careful study was made of the background of every patient, including examination of records going back to the time of army or navy service and a complete physical examination by a competent physician. There were routine examinations of the eyes, the ears, the nose, the throat, the skin, the genito-urinary system and the teeth. A routine Wassermann test was made for every patient. Every patient with a positive Wassermann reaction and every patient who was clinically suspected of having syphilis but for whom the laboratory found a negative Wassermann reaction had another test performed as a check at the National Institute of Health. Further examinations were made by consulting specialists in cases in which such examinations were indicated, and other laboratory work was done and roentgenograms were taken as needed.

Table 1 shows the location of the lesions of leukoplakia buccalis. In the majority of cases the buccal mucosa was involved, either alone or in association with other parts of the mouth. In 18 cases the location was not accurately given.

Of the 327 patients 276, or 83.79 per cent, used tobacco. Forty-eight smoked pipes; 18 smoked cigars; 7 chewed tobacco, and 203 smoked cigarets. In 46 cases there were no accurate data on the use of tobacco. Five patients, or 1.5 per cent, did not use tobacco in any form, according to their statements.

The only constitutional disease that has been consistently associated with leukoplakia is syphilis. Among the 16,802 veterans examined, there were 622, or 3.6 per cent, for whom a definite diagnosis of syphilis was made. Among the 327 patients with leukoplakia there were 33, or 10 per cent, with syphilis. Thus, it will be seen that

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syphilis occurred three times as frequently among the patients with leukoplakia. Among these there were 31 additional patients who probably had syphilis, as indicated by previous partially positive Wassermann test. This would indicate a probable incidence of syphilis of 19.57 per cent among patients with leukoplakia, but as no comparable figure is available for the whole group, this figure cannot be used for comparison.

However, if the larger figure, of almost 20 per cent, is accepted as representing the real incidence of syphilis in the group of patients with leukoplakia, there were 80 per cent of the patients for whom a most painstaking examination showed absolutely no evidence of syphilis. It seems to me that this is conclusive evidence that syphilis plays a minor role in the causation of leukoplakia. On the other hand,

TABLE 1.—*Location of Lesions of Leukoplakia Buccalis*

Buccal mucosa	217
Buccal mucosa and lips	29
Buccal mucosa and gums	1
Buccal mucosa and tongue	2
Buccal mucosa, tongue and lips	3
Buccal mucosa, lips and palate	1
Buccal mucosa and palate	3
Buccal mucosa, gums, lips and tongue	1
Gums	3
Gums and tongue	1
Lips	38
Palate	2
Tongue	8
	309
Mouth (location not stated)	18
	327

as syphilis was three times as frequent among the patients with leukoplakia, it must be conceded that syphilis probably does act as a background for the development of this disease. I am convinced from observation of individual cases that syphilis plays an important part, particularly in cases of leukoplakia of the tongue.

Because of the pathologic similarity between syphilis and tuberculosis, it was thought that a study of the latter disease might be of interest. Of the 33 syphilitic patients, 7 had tuberculosis. There were 2,408 cases of tuberculosis, or 14.3 per cent, among the 16,802 veterans examined. In the group with leukoplakia, 39 patients, or 11.92 per cent, had tuberculosis. It is thus apparent that tuberculosis is not a causative factor in cases of leukoplakia.

The condition of the mouth and teeth is naturally a possible factor in the production of leukoplakia. Table 2 shows in detail the various dental diagnoses in a comparison between the group as a whole and the group with leukoplakia. While the incidence of pathologic dental conditions was higher in the group with leukoplakia, the difference was

not large enough to have any special significance. The figures in column 4, for the patients with leukoplakia and syphilis, are surprising because they are relatively lower than those for the whole group, but this is probably not significant.

The possibility that focal infection in the nose, the throat or the respiratory tract might play a part in the causation of leukoplakia was considered. Table 3 shows the detailed findings in the group as a whole and in the group with leukoplakia. There was about 20 per cent more of this type of infection in the group with leukoplakia. This difference is sufficient to be noticeable but hardly enough to justify making it the basis for any definite conclusions. A similar study of general diseases and infections shown in table 4 fails to show any significant differ-

TABLE 2.—*Dental Diagnosis*

Diagnosis	Total Group of 16,802 Veterans	Group of 327 Patients with Leukoplakia	Group of 39 Patients with Tuberculosis Among Those with Leukoplakia	Group of 33 Patients with Syphilis Among Those with Leukoplakia
Abscessed teeth	5,891	136	18	8
Abrasion	547	4	0	1
Calculus	6,428	184	22	11
Caries	8,796	211	24	15
Deciduous teeth	11	1	0	0
Erosion	139	1	0	0
Gingivitis	6,329	173	17	10
Impacted teeth	578	6	0	0
Nonvital teeth	2,180	31	1	0
Pyorrhea	4,795	148	20	11
Unerupted teeth	33	1	0	0
Total	35,727	896	102	56
Percentage of dental deficiency	212.6	274	261.5	169.6

ence. Tables 3 and 4 together show a somewhat greater susceptibility to infectious and irritative processes for patients with leukoplakia. The only conclusion one may possibly draw from this is that the patients with leukoplakia were more susceptible to other diseases than their fellows.

RELATION OF LEUKOPLAKIA TO CARCINOMA

Leukoplakia has long been recognized as a possible soil for the development of carcinoma in the oral cavity. Among the 16,802 veterans examined, carcinoma of the oral cavity was encountered on the lips in 19 cases, on the cheek in 1 and in the larynx in 6. In only four of these—3 in which the lip and 1 in which the buccal mucosa were involved—was the carcinoma directly associated with the leukoplakia. Of the 6 patients with carcinoma of the larynx, 4 had leukoplakia of the mouth, but the records failed to state whether there was any leukoplakia in the larynx.

The direct association of cancer with leukoplakia in only 4 of the 327 cases, the presence of leukoplakia in only 4 of 41 cases of cancer in the mouth itself and the absence of any evidence of leukoplakia in 19 cases of carcinoma of the tongue do not indict leukoplakia as a com-

TABLE 3.—*Foci of Infection of the Ear, Nose, Throat or Respiratory Tract*

Diagnosis	Total Group of 16,802 Veterans	Group of 327 Patients with Leukoplakia	Group of 39 Patients with Tuberculosis Among Those with Leukoplakia	Group of 33 Patients with Syphilis Among Those with Leukoplakia
Bronchitis	1,589	48	7	2
Bronchiectasis	58	3	1	2
Otitis media	2,181	48	3	4
Otitis interna	1,248	37	4	7
Tonsillitis	3,020	57	9	4
Sinusitis	1,030	24	3	3
Rhinitis	489	16	2	3
Pharyngitis	1,216	34	2	4
Nasopharyngitis	35	1	0	0
Cobblestone tongue	1	1	0	1
Laryngitis	558	13	1	1
Total	11,425	282	32	31
Percentage of infection in the ear, nose, throat or respiratory tract	67.9	86.2	82	93.3

TABLE 4.—*General Foci of Infection*

Diagnosis	Total Group of 16,802 Veterans	Group of 327 Patients with Leukoplakia	Group of 39 Patients with Tuberculosis Among Those with Leukoplakia	Group of 33 Patients with Syphilis Among Those with Leukoplakia
Arthritis	1,782	34	4	5
Arteriosclerosis	1,572	28	1	4
Cardiovascular-renal disease	11	1	0	0
Cholecystitis	221	6	0	0
Colitis	467	14	3	2
Diabetes insipidus	10	1	0	0
Diabetes mellitus	15	5	0	0
Enterocolitis	14	1	0	0
Epididymitis	137	4	1	1
Gastro-enteritis	8	1	0	0
Hepatitis	62	1	0	1
Nephritis	263	4	0	0
Osteo-arthritis	299	15	1	0
Proctitis	29	1	0	0
Prostatitis	942	22	0	0
Pyelonephritis	20	1	0	0
Raynaud's disease	21	2	0	1
Renal changes	1	1	0	0
Seminal vesiculitis	72	2	0	0
Sigmoiditis	9	1	0	0
Stomatitis	30	1	0	0
Duodenal ulcer	209	4	0	0
Urethritis	219	12	3	2
Total	6,413	162	13	16
Percentage of general foci of infection	38.1	49.5	33.3	48.4

mon precancerosis. However, the group studied consisted of patients who had just reached the age at which cancer might be expected to be common. Perhaps ten years or more from now the incidence of cancer among these same 327 patients will be much higher.

SUMMARY AND CONCLUSIONS

Among 16,802 patients examined, 327, or 1.9 per cent, had leukoplakia buccalis.

Tobacco was used by all but 5 of the 327 patients.

Syphilis was three times as common among the patients with leukoplakia as it was among the whole group. Nevertheless, syphilis could be entirely excluded in over 80 per cent of the cases. I do not believe, therefore, that syphilis is an important factor in the etiology of leukoplakia.

Infections of the mouth, the ears, the nose, the throat, the respiratory tract and other common sites of infection were somewhat more prevalent among patients with leukoplakia, but there was not enough difference to attribute any etiologic importance to these factors.

Of 327 cases of leukoplakia, carcinoma involved the lip in 1, the cheek in 1 and the larynx in 6. In only 4 of these, however, was carcinoma directly associated with the lesion of leukoplakia.

It is probable that leukoplakia is the result of an inherent tendency to hyperkeratosis following local irritation, and not of any constitutional disease.

Dr. Blanche Wilcox assisted in preparing the statistical data.

ABSTRACT OF DISCUSSION

Dr. Howard Fox, New York: As the essayist's report dealt entirely with men, the question of the rarity of leukoplakia buccalis among women was not discussed. In a report on leukoplakia buccalis a number of years ago I quoted the statement of Cumston that of 838 cases of leukoplakia collected from the literature in only 30 were women affected. The rarity of leukoplakia among full-blooded Negroes is not so definitely established. In a long experience with Negroes in the city of New York and in the tropics I can recall only a few cases of leukoplakia buccalis involving full-blooded Negroes. There seems to be great variation in different reports regarding the incidence of syphilis preceding leukoplakia. The incidence of 80 per cent recorded by Fournier is much too high. My own findings, however, were considerably higher than those of Dr. Eichenlaub. There can be no doubt, I think, of the relationship of leukoplakia and carcinoma. It is probable that in later years the incidence of cancer in the essayist's patients will be much higher than it is at present.

Dr. James H. Mitchell, Chicago: I wish to ask one question in regard to syphilis. Levaditi, who believed in the dual nature of the syphilitic virus, said that the syphilitic virus of the central nervous system was a sclerosing strain. It is a common observation that leukoplakia goes along with syphilis of the central nervous system, and I wish to ask what percentage of the patients studied by Dr. Eichenlaub had syphilis of the central nervous system.

Dr. C. Guy Lane, Boston: Dr. Eichenlaub commented on the appearance of carcinoma in connection with leukoplakia. Dr. A. M. Greenwood and I have had the unusual opportunity, at the Collis P. Huntington Memorial Hospital in Boston, of observing a number of cases from the standpoint of the relation of syphilis

to leukoplakia. S. H. Sturgis and C. C. Lund recently reported cases of precancerous conditions of the mouth with reference to the development of malignant growths (Leukoplakia Buccalis and Cancer, New England J. Med. **212**:7, 1935). There were 250 instances of precancerous lesions of the lip and the mouth, and of these the lesion became malignant in 25 during observation. Sturgis and Lund reviewed these cases with reference to age, sex, use of tobacco and oral hygiene, the usual factors of etiologic importance with reference to the development of carcinoma. According to their survey, these factors were of no assistance in predicting whether a precancerous lesion would become malignant. In the 25 cases in which malignant growths developed, these factors did not appear to have any significance so far as the development of malignancy was concerned.

It is interesting that the cause of death in most cases of the group studied by Sturgis and Lund fell under one of three headings: (1) delay in reporting for treatment, (2) inadequate treatment of early lesions and (3) an error in diagnosis. One or more of these preventable factors, as Sturgis and Lund have called them, led to the poor results in these individual cases. As of less importance, these authors mentioned early metastasis, usually the result of delay on the part of the patient rather than true early metastasis; extent of premalignant lesions; degree of malignancy, and the presence of multiple malignant growths. Therefore, it seems to me that two things are important: (1) education of laymen on observation and reporting and (2) education of physicians regarding adequate diagnosis and following up of patients with leukoplakia and regarding adequate and early treatment of lesions as they develop.

Dr. Harry E. Alderson, San Francisco: I think the age factor is of great importance in these cases. I see all the veterans at the Veterans Administration Facility in San Francisco. These men are almost all in their forties, and some of them, on account of poor economic conditions and sickness, have become hospitalized. Many of them have neglected their mouths and show evidences of poor oral hygiene. Manifestations of late syphilis are frequently seen, but not many patients have leukoplakia and syphilis. In cases in which the disease is mild I have occasionally seen the condition clear up after discontinuance of the use of tobacco and of the strong mouth washes which patients secure from druggists.

Dr. Erich Hoffmann, Bonn, Germany (by invitation): I agree that syphilis is not an important factor in the causation of leukoplakia. Its importance has been lessened since the introduction of the use of arsphenamine, which reduces the frequency of relapses in the mucous membranes.

Dr. H. J. Parkhurst, Toledo, Ohio: I feel that the two important factors in cases of leukoplakia are the presence in the mouth of jagged, rough teeth and the exposure of the lower lip to the rays of the sun.

Dr. F. J. Eichenlaub, Washington, D. C.: With regard to the question of syphilis, Dr. Fox believes that syphilis was present in 60 per cent of his cases of leukoplakia. While only 10 per cent of my 327 patients with leukoplakia were proved to have syphilis at the time of examination, there was almost another 10 per cent who were believed to have syphilis but for whom its presence could not be proved. Nevertheless, in 80 per cent of the cases syphilis was entirely ruled out by thorough examinations.

I cannot answer Dr. Mitchell's question, because the figures were not broken down according to type of syphilis.

Dr. Lane's remarks about carcinoma are interesting, but I can reply only by reference to the figures I gave. I expect the incidence of carcinoma in these patients to be higher in later years.

With reference to oral hygiene, that subject was covered in the discussion of the incidence of dental disability in the patients with leukoplakia and in the control group. There did not seem to be enough difference between the two groups to justify attaching any significance to the figures. The patients had no jagged teeth when I saw them, for they had been admitted to different hospitals at various times and had had the teeth removed. In most cases the leukoplakia was not on the tongue, but I saw no associated glossitis among those patients whose tongues were involved. I have had 3 private patients with glossitis and leukoplakia, all of whom were syphilitic.

Exposure to the sun may have been a factor in cases in which the lip was involved, but in most cases under consideration the disease was inside the mouth, and there could be no question about exposure to the sun as a factor in these cases.

ACQUIRED SPECIFIC HYPERSENSITIVITY TO SIMPLE CHEMICALS

II. CHEILITIS, WITH SPECIAL REFERENCE TO SENSITIVITY TO LIPSTICK

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The various inflammatory conditions of the vermilion border of the lips are usually called "cheilitis" with varying qualifying adjectives. Since the vermilion border is embryologically closely related to the skin, it is not unexpected that the majority of cutaneous diseases may affect the transitional membranes of the lips.

The differential diagnosis of inflammatory processes of the vermilion border must include such common cutaneous diseases as lupus erythematosus, erythema multiforme, drug eruptions, pemphigus, lichen planus and lupus miliaris disseminatus faciei. While certain cutaneous diseases, such as psoriasis, seborrheic eczema and pityriasis rosea, rarely if ever localize on the lips, other diseases, including herpes simplex, bullous erythema multiforme, certain drug eruptions, angioneurotic edema and syphilitic chancres and papules, show a predilection for this region. In addition, there are certain so-called idiopathic superficial and deep pathologic alterations which usually appear solely on the lips. These include cheilitis exfoliativa and cheilitis glandularis.

At the beginning of our investigations we believed that these classic types of cheilitis would account for the majority of labial involvements among the subjects studied. However, our studies have now convinced us that in our patients—seen in both office and clinic—cheilitis due to

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sensitivity to contact substances, particularly to lipstick, today plays the the most important role.[1]

We do not wish to deny the existence of so-called idiopathic cheilitis, such as cheilitis exfoliativa. However, during the two years of our investigation we have found no cheilitis which when adequate study was possible could not either be classified as a manifestation of some other known dermatosis or be proved due to exposure to contact substances or physical agents (light, trauma, biting, licking, etc.).

In our series there were only two (inadequately studied) cases of cheilitis—that of a man aged 31 and that of a girl aged 14—in which we were unable to determine the etiology. In the case of the girl a metal dental brace was suspected as the cause. While in both of these instances we may have been dealing with idiopathic cheilitis, it is nevertheless possible that proper investigation might have revealed the causal factor.

A third case was that of a nun aged 39, who had suffered for two months from severe cheilitis of both the upper and the lower lip, with some dermatitis on the adjacent skin. While the appearance of this cheilitis was identical with that which may be produced by lipstick and which is described later, both lipstick and other cosmetics could be definitely excluded as causal factors in this case. Investigation by means of patch tests revealed a positive reaction to a proprietary tooth-paste containing menthol, saccharin, glycerin, powdered tragacanth, powdered soap, precipitated calcium carbonate, oil of clove, oil of cinnamon, oil of peppermint, methyl salicylate, sassafras, eucalyptol, oil of anise, red coloring materials and water. Unfortunately, we were unable to determine which of these ingredients produced the cheilitis. However, avoidance of the tooth-paste led to a complete and lasting cure.

It is noteworthy that not only in cases in which the condition was due to lipstick but in this particular case, in which the cheilitis was caused by a substance employed not on the lips but actually within the mouth, no stomatitis, gingivitis or glossitis was present.[1] Sensitivity of the mucous membranes to contact substances is extremely rare, although several cases of sensitivity of the mucous membranes to contact substances have recently been reported, including one of sensitivity to lipstick.[2]

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1. For early reports of cheilitis due to allergic sensitization, see: Neisser, A.: Lippenekzem und Mundwässer, Deutsche Monatschr. f. Zahnh. **9**:420 (Feb.) 1898. Jadassohn, J.: Einige Bemerkungen zum Odolekzem, Zentralbl. f. Haut- u. Geschlechtskr. **7**:158, 1922.

2. (*a*) Sainz de Aja, E.: Glositis y queilitis artificial (caso clinico), Actas dermo-sif. **21**:549 (May) 1929. (*b*) Rattner, H.: Stomatitis Due to Sensitization to Dental Plates, J. A. M. A. **106**:2230 (June 27) 1936. (*c*) Loveman, A. B.: Stomatitis Venenata: Report of a Case of Sensitivity of the Mucous Membrane and the Skin to Oil of Anise, Arch. Dermat. & Syph. **37**:70 (Jan.) 1938.

The picture of cheilitis based on hypersensitivity to lipstick and other contact excitants is fairly uniform, although not absolutely diagnostic (fig. 1). The eruption is confined, as a rule, to the vermilion borders and to a narrow margin of the immediately adjacent skin. Sometimes the transitional mucosa alone is involved, the surrounding skin remaining entirely unaffected. Occasionally the principal seat of the disease is not the vermilion portion but a narrow margin of the true skin adjacent to it.

The manifestations usually consist of more or less swelling and scaling. In some instances the lips are slightly edematous and extremely dry and present only an accentuation of the normal markings. In others there are marked scaling and even fissuring, with occasional superficial erosions. In one case, that of a brunette girl, there was

Fig. 1.—Severe cheilitis proved to be due to lipstick. In spite of a demonstration of a high degree of local hypersensitivity of the lips, the skin of this patient was in general not sensitive, showing no reactions to repeated patch tests with the offending lipstick and its ingredients. However, tests of the lips gave positive results and permitted the final selection of an innocuous substitute for lipstick.

definite hyperpigmentation, which gave the lips a bluish appearance, suggesting cyanosis. This discoloration, which disappeared slowly in the course of several months, was confined to the everted portions of the vermilion border, the juxtaposed portions being of normal color even though they presented evidence of cheilitis. This finding made us suspect the possible role in some cases of photosensitization, as reported by Gougerot.[3] With the majority of our patients repeated close observation revealed stages in which pinpoint-sized, closely agminated vesicles could be seen. Sometimes a fine, narrow margin beyond the vermilion

3. Gougerot, H.: Chéilitis solaires. Lucites solaires labiales et causes sensibilisantes, Bull. Soc. franç. de dermat. et syph. **43**:1592, 1936.

border exhibited slight swelling, erythema and minute vesicles. The scaling varied from scarcely visible, fine adherent scales to large patches of desquamation. The involvement always included both the upper and the lower lip in their entire length; there was no favoring of either the central portions or the lateral angles. The buccal surface was always spared.

Without exception the patients complained of subjective manifestations, such as dryness, burning and tingling. There was, however, great variation from case to case in the severity of these symptoms.

In the majority of our cases the condition appeared shortly after the use of a new type or brand of lipstick, but in a few instances the symptoms appeared while the patient was using a brand of lipstick which had been used for many years or even while she was using the same lipstick which had been used for many months previously without irritation. The usual inception of cheilitis consisted of slight dryness and so-called chapping of the lips. This was followed—sometimes only after many months of continued use of the same lipstick—by the more pronounced manifestations previously described.

In some of our cases a few hours' wearing of the offending lipstick after one application was sufficient to produce subjective and objective manifestations lasting several weeks. In one case we observed continuations of the manifestations and flare-ups for seven weeks after the last application of the lipstick. In another case the manifestations subsided regularly within two or three days after the last application.

It is well known that cheilitis may be caused by sensitivity to the ingredients of lipstick. For more than a decade both in the American and in the European literature [4] there have been frequent reports of such cheilitis. The first American report we have encountered is that of Miller and Taussig [4a] in 1925. Few authors have made the attempt to analyze the sensitivity and to ascertain the constituents of the lipstick which are responsible for cheilitis. In fact, in the earlier reports the emphasis was placed more on poisoning than on idiosyncrasy and sensi-

4. (*a*) Miller, H. E., and Taussig, L. R.: Lipstick Dermatitis Due to Carthamine and Eosin, J. A. M. A. **84**:1999 (June 27) 1925. (*b*) Audry, C., and Valdiguié: La chéilite du rouge, Bull. Soc. franç. d. dermat. et syph. **35**:623, 1928; (*c*) Sur le rôle de l'éosine dans le chéilite du rouge, ibid. **35**:923, 1928. (*d*) Sainz de Aja.[2a] (*e*) Kling, A.: Accidents causés par les teintures organiques utilisées pour les chaussures, étoffes, fourrures, ainsi que la préparation de certaines fards, Bull. Acad. de méd., Paris **103**:640, 1930. (*f*) Lain, E. S.: Cosmetic Eruptions, South. M. J. **25**:718 (July) 1932. (*g*) Carleton, Alice: Uses and Dangers of Cosmetics, Brit. M. J. **1**:999 (June 10) 1933. (*h*) Baer, H. L.: Lip-Stick Dermatitis, Arch. Dermat. & Syph. **32**:726 (Nov.) 1935. (*i*) Sézary, A.; Horowitz, A., and Genet, H.: Chéilite du rouge (intolérance à l'éosine) chez une malade intolérante à la lanoline, Bull. Soc. franç. de dermat. et syph. **43**:1542, 1936. (*j*) Sézary, A., and Horowitz, A.: La chéilite du rouge, Presse méd. **45**:137 (Jan. 27) 1937.

tization. In 1924 Cole,[5] for example, discussed the deleterious effects of lead and mercury in cosmetics. It is obvious that at present poisoning from heavy metals is not a factor in the cheilitis due to lipstick, for there must be few if any cosmetics which still contain these metals in amounts sufficient to be of toxicologic significance.

Therefore, in considering irritations produced by lipstick one must today regard all the ingredients as possible sensitizers rather than as poisonous substances in the toxicologic sense.

The first step in such a consideration is necessarily to ascertain the usual composition of the modern lipstick. The lipstick in common use

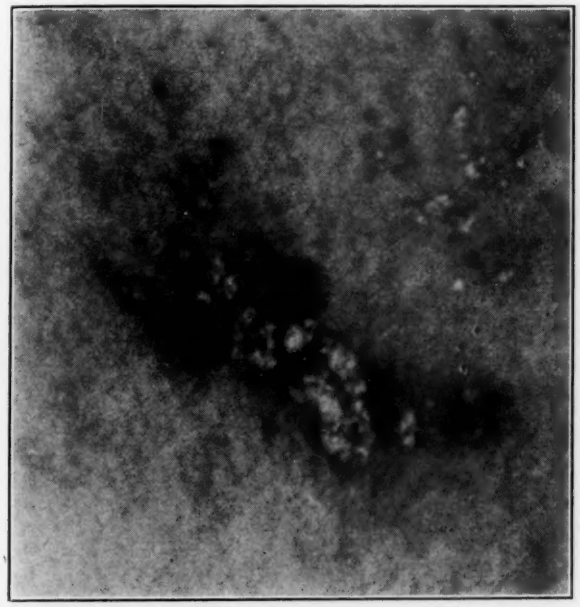

Fig. 2.—A positive reaction to a patch test with lipstick in a patient with lipstick cheilitis.

has a fatty base, commonly containing several of the following ingredients: yellow wax, paraffin, petrolatum, hydrous wool fat, castor oil, stearic acid and cetyl alcohol. Further details will be found in the paper by Baer.[4h] In this base are incorporated perfumes, dyes and lakes.

In our cases many different varieties and makes of lipstick were responsible for the clinical manifestations. One patient suffered recurrences of the cheilitis after the use of each of eight different brands. In the cases here reported fourteen different makes of lipstick produced positive reactions to patch tests (figs. 2 and 3). Since it was impossible to ascertain the exact composition of each lipstick, our studies consisted

5. Cole, H. N.: Dermatoses Due to Cosmetics, J. A. M. A. **82**:1909 (June 14) 1924.

mainly of the endeavor to find substances which could be used to form a substitute lipstick which would be innocuous for the individual patient.

Eight patients were given patch tests with five ingredients commonly used in the bases of lipsticks, namely, yellow wax, paraffin, petrolatum,

Fig. 3.—Positive vesiculobullous reactions to patch tests with two indelible dyes in a patient with lipstick cheilitis.

stearoricinol (a combination of stearic acid and castor oil) and cetyl alcohol. These tests revealed no definite eczematous hypersensitivity of the skin. Questionable reactions were encountered in a few cases, but even in these subsequent observation proved that the cheilitis was

not attributable to an ingredient of the base. While we did no patch tests with hydrous wool fat, in all the cases here reported there was definite hypersensitivity to dyes, so that there was no evidence pointing to that constituent of the base as a principal factor. However, as reported by Morse and one of us,[6] marked eczematous hypersensitivity to hydrous wool fat does exist; other cases of this form of hypersensitivity have recently been reported.[7]

In one case, nevertheless (no. 8, table 1), in spite of absence of reactions to patch tests, slight scaling of the lips resulted from a few days' use of an unperfumed and uncolored lipstick base. This exceptional case will be discussed in greater detail later in the report. We are satisfied that in our series the existing hypersensitivity was not due to the base, although it is possible that the ingredients of the base may have played a part in producing sensitization to other constituents of the lipstick (either by acting as primary irritants or by serving as the large molecular constituent conferring sensitizing power on a hapten).

Perfume was found responsible in only one of our cases (no. 11, table 1). Even in this instance it was apparently not the sole factor, since the patient experienced a recurrence of cheilitis while she was using a nonperfumed lipstick and showed positive reactions to patch tests with several dyes. In considering perfume as a factor, we naturally focused our attention to a great degree on methyl heptine carbonate. Baer [4h] reported this substance to be the causal factor in his case of cheilitis caused by lipstick. In another instance Hoffman and Peters [8] attributed to methyl heptine carbonate a dermatitis of the face resulting from the use of a facial cream. In addition, Landsteiner and Jacobs [9] have reported that the skins of guinea pigs could be sensitized to methyl heptine carbonate by repeated injections of 0.05 cc. of a 1 per cent solution of this substance in olive oil.

In view of the findings mentioned, it is rather astonishing that in not one of our cases of lipstick cheilitis could the condition be shown to be due to methyl heptine carbonate.[10]

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6. Sulzberger, Marion B., and Morse, J. L.: Hypersensitiveness to Woolfat, J. A. M. A. **96**:2099 (June 20) 1931.

7. (*a*) Milian, C., and Garnier, G.: Dermatose des tondeurs de mouton, Bull. Soc. franç. de dermat. et syph. **43**:1473, 1936. (*b*) Sézary, A., and Horowitz, A.: Intolérance cutanée à la lanoline, ibid. **43**:1544, 1936.

8. Hoffman, M. J., and Peters, J.: Dermatitis Due to Facial Cream, Caused by Methyl Heptine Carbonate, J. A. M. A. **104**:1072 (March 30) 1935.

9. Landsteiner, K., and Jacobs, J.: Sensitization of Guinea Pigs with Methyl Heptine Carbonate, J. A. M. A. **106**:1112 (March 28) 1936.

10. One of the largest manufacturers of lipstick in this country informed us that immediately after Baer's report was published methyl heptine carbonate was eliminated from his products.

TABLE 1.—*Results of Making Patch Tests on Fourteen Patients with Hypersensitivity to Lipstick with Twenty Dyes Commonly Used in Lipsticks*

Patients / Dye No.	1 K.	2 G. O.	3 S. H.	4 E.	5 G. A.	6 G. R.	7 B. L.	8 D.	9 F.	10 M.	11 B.E.	12 J.	13 S. C.	14 F. E.	Total Reactions +	2+	3+	Total
1	0	0	++	0	0	++	0	0	+†	0	+(+)	(+)/+	+/+	+-++/?	3	4	0	7
2	0	0	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	+	0	0	0	0	0	0	0	0	1	0	0	1
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	0	?	?	0	0	0	0	0	0	0	0	?	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	?	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0/+++/0	+	+/0	2	0	1	3
9	0	0	0	+	0	0	0	0	0	0	0	0	0	0	1	0	0	1
10	0	0	0	?	0	0	0	0	0	0	0	0	0	+/?	1	0	0	1
11	0	0	0	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	+	0	0	0	0	0	0	0	0	0	0	1	0	0	1
13	0	0	0	+	0	0	0	0	0	0	0	0	0	0	1	0	0	1
14	0	0	0	++	0	0	0	0	0	0	0	0	++	+++/?/+	0	2	1	3
15	0	0	+	++	0	0	0	0	0	0	0	0	+++	++/?/0	1	2	1	4
16*	+	0	0	++	0	0	0	0	0	0	+	+	0	0	3	1	0	4*
17*	+	0	0	++	0	0	0	0	0	0	0	++	0	0	1	2	0	3*
18*	+-++	0	?	+++	+‡	0	++-+++	0	0	0	+	++	0	0	2	2	2	6*
19*	+-++	0	0	+++	0	0	++-+++	0	0	0	?	++	0	0	0	2	2	4*
20*	++	0	?	++	++	?0	+++	0	0	0-?	+	++-+++	0	0	1	3	2	6*
21*	..	..	+	..	+	+	..	..	..	..	+	++	0	0				

* Indelible dyes.
† Dec. 26, 1935, delayed; Feb. 26, 1936, forty-eight hours.
‡ Delayed reaction.
Readings separated by a hyphen indicate reactions falling between two readings (as ++-+++ = between 2 and 3 plus). Readings separated by / indicate results of repeated tests. +(+) indicates a 1 to 2 plus reaction (high degree of erythema but no papules). (+) indicates a slight degree of erythema, less than that recorded by +.

In order to determine whether cutaneous hypersensitivity to methyl heptine carbonate could be demonstrated in any of our patients by means of patch tests, it was necessary first to determine whether solutions of this substance might be primary irritants and, if so, in what dilutions methyl heptine carbonate would prove innocuous to normal skins. In patch tests on ninety-five control subjects without cheilitis, including both men and women, it was found that concentrations of 30 per cent, 20 per cent and 10 per cent in 70 per cent alcohol were too strong and produced reactions of primary irritation in the majority of the patients to whom they were applied. A concentration of 1 : 400 was found to produce reactions in four of fifty subjects tested. Three of these reactors showed reactions to dilutions as high as 1 : 10,000. A further series of twenty-nine men and women, all without cheilitis, were tested with concentrations ranging from 1 : 5,000 to 1 : 1,000,000. Only one subject showed reactions, and these appeared with all dilutions employed. These experiments demonstrate that concentrations stronger than 1 : 400 do not seem to be suitable for patch tests in investigating the contact type of eczematous hypersensitivity to methyl heptine carbonate.

Since the concentration of methyl heptine carbonate used in cosmetics is undoubtedly much less than 1 : 400, and since all our reacting and demonstrably hypersensitive patients responded to dilutions of 1 : 10,000 or greater, it would seem advisable not to attach clinical significance to reactions to patch tests with concentrations greater than 1 : 10,000.

After thus determining the concentration of methyl heptine carbonate suitable for the demonstration of true eczematous hypersensitivity, we were able to give patch tests properly to eight patients who were sensitive to lipstick. All showed negative reactions to the 1 : 10,000 dilution —a finding which substantiated clinical evidence exculpating perfume as a factor in all but the one subject previously mentioned. This one patient (case no. 11, table 1), although sensitive to the blend of perfume in her lipstick, was not hypersensitive to methyl heptine carbonate and showed no reaction to patch tests with the substance even with concentrations as strong as 1 : 400.

We are satisfied that in our series the existing hypersensitivity was in no instance directed toward the methyl heptine carbonate and that, with one exception, it was not directed toward any other ingredient of the perfume. It is possible, however, that the perfume, like the base, may be a factor in producing hypersensitivity to other constituents.

While sensitivities to the perfume and to the base of the lipstick undoubtedly play roles in some irritations of the lips, there can be little doubt that the main sensitizing ingredients—and thus the main causes of lipstick cheilitis—were in our cases the dyes and lakes. Our investigation of this factor was based on tests with a group of twenty dyes and lakes commonly employed in lipsticks. In addition, certain

patients were tested with eosin (tetrabromofluorescein). All available information concerning the composition of these materials, as well as the "Colour Index" numbers,[11] is given in table 2. It will be noted that some of these colors are unprecipitated dyes, while others are precipitated on various bases. It is possible that precipitation on these bases may constitute a factor either favoring or inhibiting the development of sensitization. This possibility requires further investigation.

In all patch tests the pure colors, as commercially prepared, were applied on a piece of linen moistened with water. Control patch tests on twenty-five subjects without cheilitis (nineteen women and six men) showed conclusively that no primary irritation was caused by making tests in this manner.

Several facts are evident on examination of tables 1 and 2. First, of fourteen patients eight showed reactions to patch tests with at least one of the six indelible dyes used in testing. (These indelible dyes are all derivatives of bromofluorescein. It is therefore obvious that the possibility of local photosensitization merits consideration in regard to irritations produced by these dyes.[3] Unfortunately, no other type of indelible dye is today available for use in lipsticks.) Second, three of these eight patients were sensitive to indelible dyes alone, whereas five showed reactions to patch tests with other pigments as well. Third, five patients showed no reactions to patch tests wth indelible dyes but reacted to tests with one or more nonindelible colors. Among these nonindelible colors, no. 1 (1-sulfobetanaphthaleneazobetanaphthol) produced seven reactions in the fourteen patients tested, so that the sensitivity to this substance seems to be almost as widespread as that to the indelible dyes. The next most frequent producers of reaction in our series were no. 15, producing four reactions; no. 14, producing three reactions, and no. 8, producing three reactions. Five other dyes (nos. 3, 9, 10, 12 and 13) produced one reaction each. Six dyes (nos. 2, 4, 5, 6, 7 and 11) produced no definitely positive reactions. (Questionable reactions were not evaluated as positive because of the particular difficulty of judging slight reactions in areas stained with the red colors employed.)

The frequency with which these dyes produced reactions may be an indication of their relative capacities for producing sensitization (sensitizing index)[12] or merely of the relative amounts and frequencies

11. Colour Index, ed. 1, Bradford, Yorkshire, Society of Dyers and Colourists, 1924.

12. Rostenberg, A., Jr., and Sulzberger, Marion B.: Some Results of Patch Tests: A Compilation and Discussion of Cutaneous Reactions to About Five Hundred Different Substances, as Elicited by Over Ten Thousand Tests in Approximately One Thousand Patients, Arch. Dermat. & Syph. **35**:433 (March) 1937.

with which they are encountered, or it may represent a combination of these factors. Further studies of this problem are urgently required.

Certain observations not evident on examination of table 1 merit discussion. In one case (no. 8) no positive reactions to patch tests could be obtained. However, the causal lipstick, certain ingredients of the base and the unperfumed base all produced varying degrees of cheilitis when applied to the lips, one by one. On the other hand, neither dye no. 4 nor petrolatum caused a reaction when applied to the lips. The patient is now using and tolerating this combination of dye and petrolatum as a substitute for lipstick. In a second noteworthy case (no. 9) patch tests with the causal lipstick and with the separate ingredients produced repeated negative results on various parts of the skin, including the "V" of the neck. In spite of this absence of cutaneous reaction, it could be shown beyond doubt that the lipstick which the patient was using produced the cheilitis. Eventually this patient showed a reaction to a patch test with dye no. 1, which, however, first appeared seven days after application of the test. When this test was repeated, the reaction appeared within twenty-four hours. Our interpretation of this finding is that the patient's skin had eventually become sensitized to dye no. 1 and that the seven day delay represented the period of incubation of sensitization. The twenty-four hour reaction represented the reaction time after sensitization had been established, analogous to previous observations with butesin picrate, etc.[13] The preparation of a substitute indelible lipstick without dye no. 1 resulted in relief of the cheilitis and freedom from irritation over a period of more than a year at the time of writing.

Although Sézary, Horowitz and Genet [41] were able to elicit positive reactions to patch tests in all their reported cases, the previously mentioned two cases of our series illustrate the fact that the lips may be sensitive while the skin does not share the sensitivity and does not react to patch tests with the substances producing the cheilitis. This makes it necessary to test the lips directly if tests made on the skin give negative results. In order to ascertain which of the individual ingredients are responsible and to eliminate these in the preparation of substitute lipsticks, repeated tests of the lips may be necessary. This procedure obviously is difficult and consumes time. It cannot meet with success without a high degree of cooperation on the part of the patient.

In addition to this difficulty, many others are encountered in the endeavor to determine the exact ingredients responsible for the lipstick cheilitis, so that suitable substitute lipsticks may be prepared. The

13. Sulzberger, Marion B., and Wise, Fred: Drug Eruptions: II. Dermatitis Eczematosa Due to Drugs, Arch. Dermat. & Syph. **28**:461 (Oct.) 1933.

TABLE 2.—*Dyes Used in Testing Patients Hypersensitive to Lipstick*

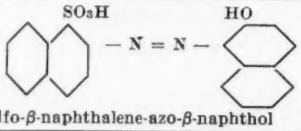
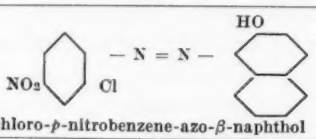
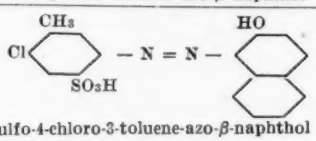
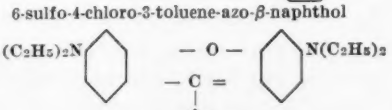
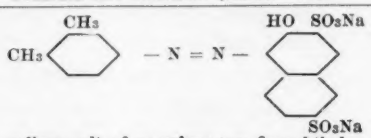
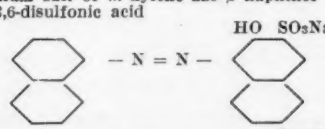
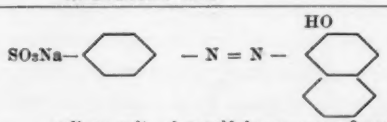
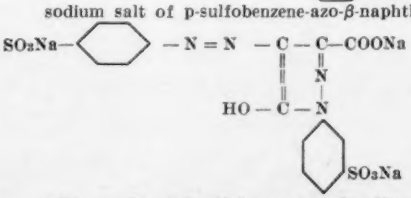
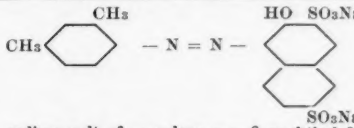
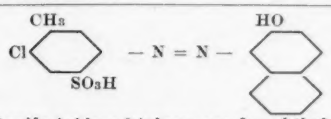
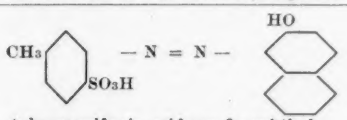
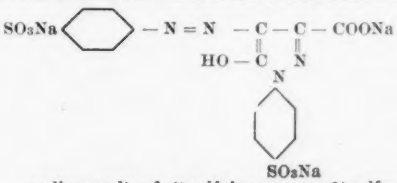
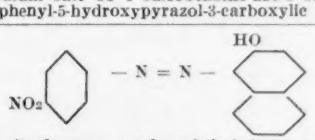
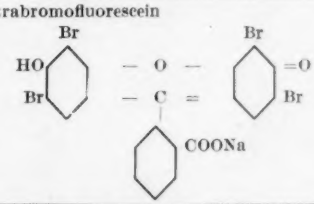
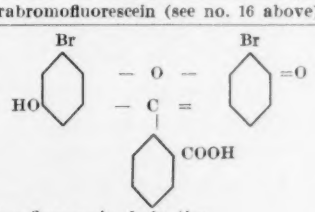
Dye No.	Color Index No.	Formula and Name	Base	Precipitants
1	189	 1-sulfo-β-naphthalene-azo-β-naphthol	$BaSO_4$	$BaCl_2$
2	Not in C.I.	Formula not available; helio-bordeaux blue	$BaSO_4$ $Al(OH)_3$	$CaCl_2$
3	.....	Acid orange lake (formula not available)	$Al(OH)_3$	$AlCl_3$ or $BaCl_2$
4	.....	 o-chloro-p-nitrobenzene-azo-β-naphthol	None	None
5	165	 6-sulfo-4-chloro-3-toluene-azo-β-naphthol		
	and		$BaSO_4$ $Al(OH)_3$	$BaCl_2$ Al benzoate
	749	diethyl-m-aminophenolphthalein hydrochloride		
6	Not in C.I.	Formula not available (athosine 3B)	$Al(OH)_3$	$BaCl_2$
7	Not in C.I.	Formula not available (athosine B)	$Al(OH)_3$	$BaCl_2$
8	79			
	and	sodium salt of m-xylene-azo-β-naphthol-3,6-disulfonic acid	$BaSO_4$ $Al(OH)_3$	$BaCl_2$ $AlCl_3$
	88	 sodium salt of β-naphthalene-azo-β-naphthol-3,6-disulfonic acid		
9	151	 sodium salt of p-sulfobenzene-azo-β-naphthol		
	and		$BaSO_4$ $Al(OH)_3$	$BaCl_2$ $AlCl_3$
	640	sodium salt of 4′sulfobenzene-azo-1′-sulfophenyl-5-hydroxypyrazol-3-carboxylic acid		

TABLE 2.—*Dyes Used in Testing Patients Hypersensitive to Lipstick—Continued*

Dye No.	Color Index No.	Formula and Name	Base	Precipitants
10	79	 sodium salt of *m*-xylene-azo-β-naphthol-3,6-disulfonic acid	$BaSO_4$ $Al(OH)_3$	$BaCl_2$ $AlCl_3$
11	165	 6-sulfo-4-chloro-3-toluene-azo-β-naphthol	$BaSO_4$ $Al(OH)_3$	$BaCl_2$
12	.....	 toluene-sulfonic acid-azo-β-naphthol	None	$BaCl_2$
13	640	 sodium salt of 4′-sulfobenzene-azo-1′-sulfophenyl-5-hydroxypyrazol-3-carboxylic acid	$Al(OH)_3$	$AlCl_3$ $BaCl_2$
14	44*	 *p*-nitrobenzene-azo-β-naphthol (para red, dark)	None	None
15	44*	See no. 14; para red, light	None	None
16	768†	tetrabromofluorescein 	None	None
17	768†	tetrabromofluorescein (see no. 16 above)	None	None
18	‡	 bromofluorescein derivative	None	None
19	‡	bromofluorescein derivative	None	None
20	‡	bromofluorescein derivative	None	None
21	.....	eosin as used for staining tissue sections	None	None

* Dyes 14 and 15 are said to be chemically the same, the difference in depth and shade being due to the difference in volume and temperature of the water and the proportion of β-naphthol and paranitraniline used in their preparation.

† Dyes 16 and 17 are said to be chemically the same. They differ only in physical characteristics, which depend on the temperature used in their preparation and the proportions of raw materials used.

‡ Dyes 18, 19 and 20 are said to be chemically the same. They differ only in physical characteristics, which depend on the temperature used in their preparation.

polyvalent sensitivities represent one confusing factor (cases 4 and 12). A second source of difficulty is that in cases of clinically identical lipstick cheilitis entirely different and unrelated ingredients are often causative. Each case must, therefore, be analyzed by careful patch tests and even "lip tests" if needed. A third difficulty became apparent in case 10. Patch tests of the patient with our twenty common lipstick dyes failed to reveal any reactions, although there was at the same time a strongly positive reaction to the lipstick which produced the cheilitis. Through the cooperation of the manufacturer of the lipstick, we were able to discover subsequently that it contained a dye not included in our series, namely, oil sudan. A patch test with oil sudan produced a strongly positive reaction. Lipsticks not containing oil sudan have now been used by this patient for six months, and there has been complete freedom from cheilitis. A fourth difficulty is illustrated by case 4, in which patch tests with the causal lipstick gave repeatedly negative results, while subsequent patch tests with undiluted dyes showed many strongly positive reactions. This was undoubtedly due to the fact that the sensitivity of the skin was less than that of the lips and was therefore demonstrable only by the application in a patch test of higher concentrations of dye than those used in the lipstick.

In cases 4, 8 and 9 the sensitivity either remained confined to the lips or existed in a much higher degree on the lips than on the skin. However, in two other cases (nos. 13 and 14) the reverse may have held true—that is, there may have been a lesser sensitivity of the lips, accompanied with a high degree of sensitivity of the surrounding skin—for in these two cases, in spite of a clinical history and course which incriminated lipstick and in spite of strongly positive reactions to patch tests with lipsticks, the irritation appeared not on the lips but on other portions of the skin of the face (the eyelids, the cheeks and the chin). Although we cannot lay claim to proof of the causal role of lipstick in these two cases, we believe that these findings indicate the necessity for considering sensitivity to lipstick as a possible cause of dermatitis in some cases in which the lips are not involved.

In this connection it may be worthy of mention that in case 9 chronic, generalized urticaria appeared during each period of use of the offending lipstick and always disappeared while the innocuous substitute was being employed (absorption or ingestion of the offending dye or dye conjugate?).

In spite of these and other difficulties, including lack of the necessary cooperation on the part of some of our patients, in six of our twelve cases of cheilitis caused by lipstick (nos. 5 to 10) we were able to supply a satisfactory substitute which produced no recurrence of the eruption during periods of observation ranging from several months

to two years. In four cases (nos. 1 to 4) of the remaining six the patient did not cooperate in returning for full testing. The two remaining cases (nos. 11 and 12) are those most recently observed. The analyses of sensitivity are not yet completed. Both patients presenting facial dermatitis possibly attributable to lipstick (cases 13 and 14) have remained free from recurrence. One is using a substitute lipstick, and the other prefers to use no lipstick at all.

Our studies have led us to the conclusion that lipstick cheilitis is caused in the main by hypersensitivity to the coloring matter in the lipstick and, as such, represents a subgroup of sensitivities to dyes in general.[14] Sensitivity to lipstick dye is therefore a matter of allergic sensitization to ordinarily innocuous dyes.

In view of the almost universal use of lipsticks by modern women, the comparative rarity of cheilitis demonstrates clearly that the dyes used must be infrequent sensitizers, capable of producing clinical sensitivity only in exceptionally predisposed persons.

SUMMARY

A short discussion of involvements of the lips is followed by a brief review of the signs and symptoms of cheilitis caused by hypersensitivity to contact excitants and, in particular, by hypersensitivity to the ingredients of lipsticks. This form of cheilitis is the most common in our material.

The study by patch tests and, when necessary, by direct testing of the lips of twelve patients with cheilitis due to lipsticks is reported in detail. A report is submitted of two cases in which there was no cheilitis but dermatitis of the face in conjunction with hypersensitivity to lipstick demonstrable by patch tests.

In the reported series hypersensitivity to ingredients of the bases of lipsticks is exculpated as the principal cause of cheilitis or dermatitis. Likewise, hypersensitivity to perfumes is not found to be responsible in the main, although one person showed hypersensitivity to perfume as well as to dyes.

Studies of methyl heptine carbonate showed that it played no part in producing cheilitis or dermatitis in this series of cases. Control tests showed that methyl heptine carbonate in a dilution of 1:10,000 in 70 per cent alcohol is a safe concentration for patch testing to demonstrate hypersensitivity.

Patch tests with dyes and pigments used in making lipsticks revealed that eight of fourteen patients showed hypersensitivity to the indelible

14. Sulzberger, Marion B., and Goodman, J.: Acquired Specific Hypersensitivity to Simple Chemicals: I. Eczematous Sensitivity to Clothing and to Cosmetics, with Special Reference to Dyes, J. Allergy **9**:136 (Jan.) 1938.

dyes (bromofluorescein derivatives) and that seven of fourteen patients showed hypersensitivity to an azo dye commonly employed in lipsticks (1 sulfobetanaphthaleneazobetanaphthol). Details of sensitivities to other dyes employed for testing and of histories of individual cases are given in the tables and discussed in the text.

In the twelve reported cases of cheilitis caused by lipstick, six patients have been provided with new substitute lipsticks which produce no cheilitis; two are still being studied, and four have not cooperated to an extent sufficient to allow the preparation of substitute lipsticks.

In view of the present widespread use of lipsticks, it may be concluded that cheilitis due to lipstick is relatively rare; when it occurs, it is usually based on an acquired allergic hypersensitivity to one or more of the dyes and pigments in the lipstick.

962 Park Avenue.

For their invaluable cooperation in furnishing materials for cutaneous tests and in preparing substitute lipsticks, the authors wish to express their thanks to Dr. Albert B. Pacini, of Jersey City, N. J.; to Mr. S. H. Ebert, of the Interstate Color Co., of New York; to Mr. William Erath, of the Ansbacher-Siegle Corp., of New York, and to the Almay Pharmaceutical Corporation of New York. For referring certain of the patients included in this study the authors wish to thank Drs. Charles R. Rein and Ludwig Schwarzschild, of New York.

ABSTRACT OF DISCUSSION

Dr. James H. Mitchell, Chicago: I saw recognized lipstick dermatitis for the first time in 1925. The patient had both cheilitis and stomatitis. She was in the hands of internists and they were unable to bring about any improvement. As a substitute for lipstick I suggested that she use mercurochrome—this is about the only thing I ever recommend it for. It serves nicely, and she rather liked it, for it stayed on well.

I am told that in Wyoming at the time of the round-up the cowboys buy up all the lipstick in town, because they know it protects the lips from the sun.

I observed another instance of the combination of irritation of the mucous membrane and cheilitis recently. The patient stated that she had marked dermatitis due to butesin picrate two years before. Recently a physician sprayed her nose and packed it with a butesin nasal spray. Not only did severe cheilitis of the lip develop, but the nasal mucous membrane and the throat were affected. She was a singer and was completely incapacitated for a month.

About two years ago I was consulted in my home and once in the office by a woman who had cheilitis which I assumed to be lipstick dermatitis, and I told her so. I learned later that the trouble was found by others to be due to her husband's mustache wax.

Dr. Fred Wise, New York: In direct connection with cheilitis of the lips and the buccal mucous membrane I wish to mention two cases of eruption of the face due to poison ivy which were complicated by intrabuccal involvement. I wonder whether others have observed intrabuccal inflammation in association with eruptions of the lips themselves and the surrounding skin due to poison ivy.

Dr. J. R. Driver, Cleveland: I wish to report an interesting case in which severe distressing cheilitis of several years' duration was due to dental plates. The patient was an elderly woman who had worn her plates for fourteen years and had had the involvement of the lips for a number of years. The hard palate was involved but not so severely as one would expect from the reaction on the lips.

An interesting thing about the patch test was that when I strapped the plate on the forearm and removed it at the end of twenty-four hours there was apparently no reaction, but within two hours a severe vesicobullous eruption appeared. Apparently exposure to the air was necessary to the production of this result. I wish to ask Dr. Sulzberger whether he has observed any cases in which exposure to the air is apparently a responsible factor in causing the reaction.

Dr. Bedford Shelmire, Dallas, Texas: It has been my experience that true sensitivity of the mucous membrane to an exogenous agent is only rarely accompanied by cutaneous sensitivity to the same excitant. The vermilion border of the lips reacts more like the glabrous skin. When I was performing patch tests with poison ivy some years ago, approximately 75 per cent of adult subjects showed cutaneous sensitization to the resinous oil of Rhus radicans. No reactions were obtained in subjects sensitive to poison ivy when the oil was painted on the mucous membrane of the oral cavity. This may have been due in some cases to the rapid dilution of the oil. In certain concentrations the oil of poison ivy acts as a direct irritant to the skin.

In listing excitants causing cheilitis one should remember vegetation. I have proved that vesicular cheilitis in one case was due to hackberry and in another to Amoor river privet, a snuff brush being the medium in each instance.

Dr. E. William Abramowitz, New York: One manufacturer of cosmetics furnished me for testing purposes a set of various ingredients, eight in all, used by his organization in making lipsticks. They were petrolatum, yellow wax, cetyl alcohol, paraffin, stearoricinol, indelible dye no. 1, colors 2, 3 and 4 and perfume.

The rhodamines are being used as dyes in some lip-sticks. These may be regarded as fluorescein derivatives which contain amide or imide groups in place of hydroxyl and oxygen groups of the fluorescein. There are various salts, like rhodamine B, 313, 6 G and rhodamine S, which are all red dyes. They are not exactly derivatives of phenolphthalein but aminophthaleins. I believe that they are not in any way capable of sensitizing the patient to phenolphthalein.

Dr. M. F. Engman Jr., St. Louis: I wish to remind Dr. Shelmire that there are other ways of coming in contact with lipstick besides putting it on the lips. I observed a case recently in which a severe involvement was caused when the patient's sweetheart changed her brand of lipstick. When she changed her brand a second time the patient was all right.

Dr. John H. Stokes, Philadelphia: I might mention the case of a husband in whom double urticarial wheals developed, two on each cheek, fifteen minutes after he was kissed by his wife, who had just used a new brand of lipstick. The wheals persisted for several hours.

Dr. Eugene F. Traub, New York: I wish to report briefly on two cases of interest in this connection which I observed recently. One was that of a young girl in whom cheilitis and dermatitis developed after some dental work in which amalgam fillings were used. This type of eruption from amalgam fillings has been previously reported, but there has been some question as to whether the condition is contact dermatitis or some other form of sensitivity. This patient visited the

dentist on three successive occasions, and each time the same reaction developed when amalgam fillings were placed in her teeth. After the most recent visit to the dentist the rash was worse than it had been previously; so she went to her physician. He believed the eruption to be impetigo and applied 5 per cent ammoniated mercury, which caused an aggravation of all symptoms. When tested she was found to be extremely sensitive to mercury. The second case was similar to the first, except that there had been only one repetition of the eruption.

DR. EARL D. OSBORNE, Buffalo: Although dyes in lipsticks undoubtedly cause cheilitis in many cases, one must not forget that the dyes in finger-nail polish may act in the same way.

I should like to ask Dr. Sulzberger if he has any data on the proportion of patients with cheilitis and of patients with inflammation of the mucous membranes of the mouth from external contacts who give positive reactions to cutaneous tests. I have had a number of cases of inflammation of the mucous membrane due to a certain tooth-paste and to preparations applied to the gums for pyorrhea. One of the latter is "oryl," which contains oil of cinnamon and oil of cloves. With this substance it was impossible to secure a positive reaction on the skin, but testing of the mucous membrane produced a definite reaction.

DR. RICHARD S. WEISS, St. Louis: Dr. M. F. Engman Sr. called my attention about a year ago to another form of cheilitis, and since then I have observed four cases. He related the instance of a woman in whom cheilitis developed from contact with orange juice. I have seen such a condition in three cases since and in one case cheilitis was due to tomato juice. It is easy to get a clue to this factor by having the patient take a glass of water and watching how he drinks it, for the lesions will appear on the area touched during drinking.

DR. MARION B. SULZBERGER, New York: I wish to thank the members for their interesting discussion. I think many of the points mentioned are covered in the body of the paper, which I could not read in toto. As brought out in the discussion, the mucous membrane differs from the epidermis in its sensitivity, and the lips are in turn different from both. The sensitivity of the lips parallels that of the mucous membrane in some cases and that of the skin in others, and sometimes the lips alone are sensitive. The results Dr. Shelmire mentioned with the seventy-five subjects he tested with poison ivy both on the skin and in the mouth, again show that it is unusual for sensitivity of the oral mucous membrane to be associated with cutaneous sensitivity. However, in exceptional cases it can be shown that the skin and the oral mucosa are both sensitive to poison ivy and to other contact excitants.

I have observed one case like the one mentioned by Dr. Engman, in which the husband had his wife change her brand of lipstick, and that stopped his cheilitis.

Regarding the question of urticaria, I am glad Dr. Stokes brought that up, because I believe that dyes may often be causes of urticarial eruptions. Two of our patients suffered from chronic urticaria, which stopped when exposure to the dye ceased. In one case a woman deliberately applied her old type of lipstick again and both cheilitis and generalized urticaria again developed.

I think it is most important to realize that dyes and dye conjugates may produce urticarial types of sensitivity, for this means that they can produce atopic dermatitis, rhinitis, asthma, etc. (R. L. Mayer: Asthma and Ekzem bei den Pelzarbeitern [Ursolasthma, Ursolekzem], *Arch. f. Dermat. u. Syph.* **158**:734, 1929). It seems that this may be of practical significance when one recalls the many opportunities for exposure to relatively large quantities of many different dyes

and dyed materials. These sensitivities to lipstick are only one relatively insignificant form of sensitivity to dye.

Unfortunately, I cannot answer Dr. Driver's question about the appearance of a reaction to a patch test after exposure to air, but I know that the sites of many patch tests remain entirely free from reaction for twenty-four or more hours, and then suddenly, within an hour or so, the reaction appears. There seems to be a definite period of latency. I know that pressure does sometimes tend to inhibit a reaction. If the patch is applied tightly, there is sometimes a lessening of the reaction. I do not know, however, whether these phenomena serve to explain Dr. Driver's interesting observation. Another possibility is that the patch test may have sensitized the site to light. This is surely an important factor in reactions to eosin, derivatives of tar, etc.

LXXX.—FURTHER STUDIES OF THE RELATION OF PITYROSPORUM OVALE TO SEBORRHEIC ECZEMA

ROY L. KILE, M.D.
AND
M. F. ENGMAN, M.D.
ST. LOUIS

Since the report [1] of the successful culture of Pityrosporum ovale (bottle bacillus of Unna) a series of observations with this organism have been reported.[2] Further studies have been undertaken; some of the previous studies have been repeated with a larger and more significant series of subjects, and further evidence is presented showing the relation of P. ovale to seborrheic eczema. Another clinical entity, blepharitis marginalis, was studied in order to determine the association of this disease with seborrheic eczema, as well as to present additional data relative to the possible pathogenicity of P. ovale.

MATERIALS AND TECHNIC

The patients used were for the most part adolescent and usually suffering from acne as well as seborrheic eczema. Not infrequently more than one type of inoculation was made on the same patient. Two types of tests, (1) scratching the skin of the chest and applying a whole culture of the organism with and without applying an ointment to the area (43 subjects) and (2) inoculation with a patient's own scales of an excoriated area on the chest (10 subjects), were controlled on adjacent skin. A sterile dry dressing was applied to the areas for the first two weeks of observation. Intradermal tests with various types of extracts of the organism (pityrosporin) were employed for 37 subjects, and

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Read before the Section on Dermatology and Syphilology at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 9, 1937.

Studies, observations and reports from the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, Department of Dermatology, service of Dr. M. F. Engman.

1. Moore, M.: Cultivation and Study of Pityrosporum Ovale, the So-Called Bottle Bacillus of Unna, Arch. Dermat. & Syph. **31**:661 (May) 1935.

2. (*a*) Moore, M., and Kile, R. L.: Pityrosporum Ovale as a Causative Agent of Seborrheic Dermatitis, Science **81**:277 (March 15) 1935. (*b*) Moore, M.; Kile, R. L.; Engman, M. F., Jr., and Engman, M. F.: Pityrosporum Ovale (Bottle Bacillus of Unna, Spore of Malassez) Cultivation and Possible Rôle in Seborrheic Dermatitis, Arch. Dermat. & Syph. **33**:457 (March) 1936.

whole cultures of organisms were inoculated into the intact skin of the scalp of 26 subjects whose scalps were clinically free from seborrheic eczema or pityriasis. Many of these patients were suffering from acne, but none showed any manifestations of seborrheic eczema.

Any scaliness or dermatitis not seen at the control site was read as a positive reaction. Many inoculations produced a brownish discoloration, which came on after the scaliness or appeared without it. The reaction was considered doubtful when only the discoloration was noted or if the patient showed a reaction but was seen only once after inoculation. The reactions usually appeared within from ten days to two weeks and gradually faded over the subsequent month. In a few instances the reactions were not noted for from four to six weeks. All patients were instructed to refrain from washing the test sites. The accompanying table 1 gives the results of these tests.

Inoculations of the scalp were performed on various types of subjects, mostly on persons in the age group subject to acne. A whole culture of the organism was rubbed onto the intact skin of the scalp. Twenty-six subjects were inoculated by this method. Eighteen complained within two weeks of itching which had

TABLE 1.—*Results of Experiments with Human Subjects*

Type of Test	Reaction			
	Positive	Doubtful	Negative	Total
Excoriation and whole culture	9	11	14	34
Excoriation and whole culture with lipid mixture	3	2	4	9
Auto-inoculation of excoriated area with scales from scalp	5	2	3	10
Auto-inoculation of excoriated area with scales from eyelids	2	1	3	6
Inoculation of whole culture into scalp clinically free from seborrhea	18	5	3	26

never previously been noted. All of these showed some scaliness at the site of inoculation, which was always the vertex, and less was noted throughout the scalp. This persisted for several months in most instances and for as much as six months on several patients. Five of the subjects had doubtful reactions; only a little scaliness and no itching were noted. Four experienced no reaction; most of these had typical acne, but several attempts failed to cause any scaliness. Perhaps their scalps did not furnish suitable soil for the growth of the organism. Two inoculations were performed on the area of alopecia in older persons. In these an excoriation was made before applying the organism, and a control test was made. Figure 1 shows the reaction noted after several weeks on one of these two subjects.

Pityrosporins (extract of the organism) were prepared as described in a previous publication.[2b] The sites of the intradermal tests were observed in twenty-four and in forty-eight hours. Of the various extracts used and previously described, only the endotoxin (ground cells frozen and thawed with distilled water) and the mixture of exotoxin and endotoxin gave reactions of any possible significance. The reactions were mild, there being noted in twenty-four hours a faint erythema, which slowly faded in the next few days. The presence of clinical seborrheic eczema or some other cutaneous eruption, such as psoriasis, did not seem to influence the reaction (table 2).

HISTOPATHOLOGIC PICTURE

In a previous publication [2b] a description of sections from the site of a markedly positive reaction was given. These sections were taken from an artificially produced lesion on the chest.

Sections of tissue were taken from the scalps of two subjects shortly after death. Both had rather marked seborrheic eczema of the scalp. These sections were stained with methylene blue and eosin and permanent mounts made. Both showed numerous organisms in the hair follicles, as well as in the horny layer (figs. 2 and 3). The organisms assumed various forms, some being of the large sclerotic type while others were of the small active type.

SEBORRHEA OF THE EYELIDS

Ophthalmologists have always associated a certain type of blepharitis marginalis with seborrheic eczema and often use the term blepharitis

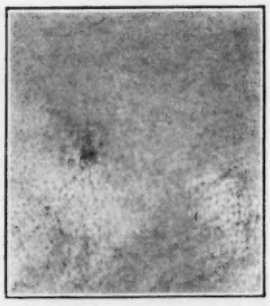

Fig. 1.—Patch of scaly dermatitis produced in the area of alopecia of an old man.

TABLE 2.—*Results of Intradermal Tests with Extracts of the Organisms*

Type of Extract	Positive*	Negative	Total
Exotoxin plus endotoxin (coccidioidin method)	13	24	37
Exotoxin (metabolic products, culture filtrate)	0	37	37
Endotoxin (ground cells frozen and thawed)	30	7	37
Exotoxin plus endotoxin (trichophytin method)	9	28	37

* A positive test was one in which erythema more than 1 cm. in diameter was seen in twenty-four hours. A tiny papule was occasionally noted.

marginalis squamosa to designate the condition. Attention has recently been called to this relationship by Van Studdiford.[3] Since this condition is so often associated with seborrheic eczema of the scalp and in many instances seems to be a manifestation of the same process about

3. Van Studdiford, M. T.: Seborrhea and Its Effect on Ocular Diseases, South. M. J. **29**:1012 (Oct.) 1936.

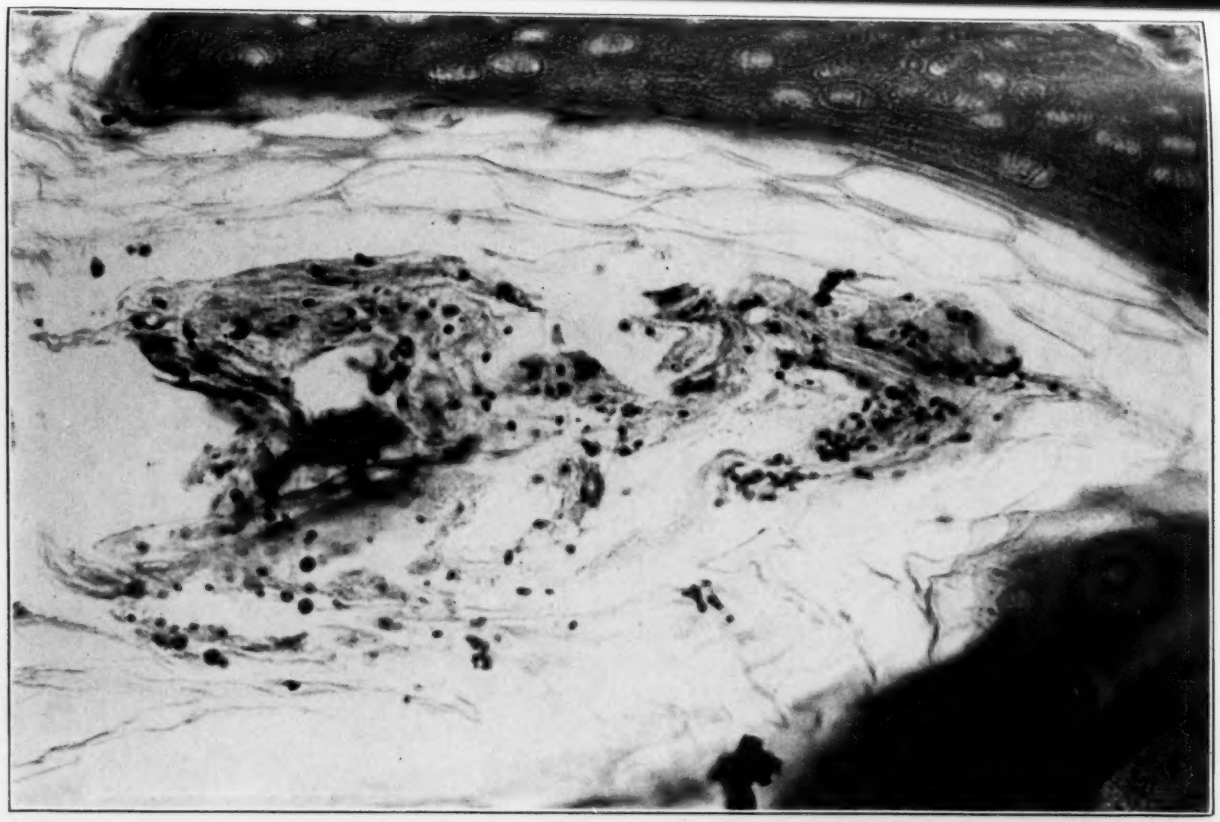

Fig. 2.—Numerous organisms (P. ovale) are seen in a hair follicle of the scalp. This section was taken shortly after death from a subject with marked pityriasis of the scalp. Methylene blue and eosin stain.

the hairs of the eyelids, it was decided to investigate this disease in a search for P. ovale. Twenty-four patients with blepharitis marginalis were studied.[4] Scales taken from the eyelids were examined for the

Fig. 3.—Organisms are seen in a scale along the surface of the skin of the scalp. This section was taken from a person shortly after death. Methylene blue and eosin stain.

4. Dr. Lawrence T. Post, chief of the ophthalmologic clinic at Washington University, gave us permission to examine these subjects.

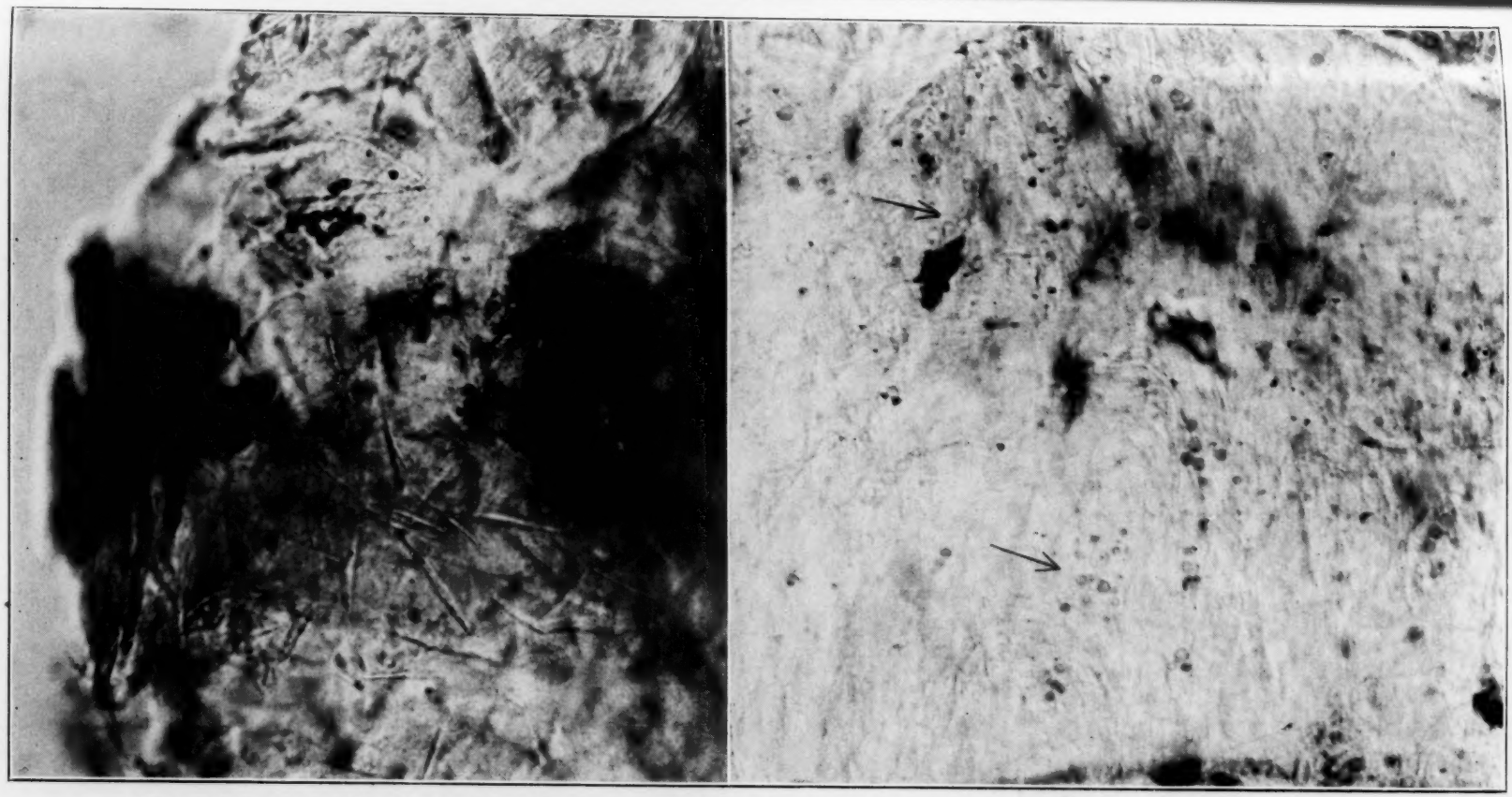

Fig. 4.—P. ovale in scales taken from eyelids of patients suffering from blepharitis marginalis. Methylene blue and glycerin mount.

organism, which was found in varying numbers in material from 21 of the 24 patients. In many instances large numbers of organisms were seen, even though a varying amount of secondary pyogenic infection was often present (fig. 4). Nearly every one of these patients also had pityriasis of the scalp. Cultures were made on wort agar (Difco) with scales from the eyelids. In numerous attempts made on 10 patients,

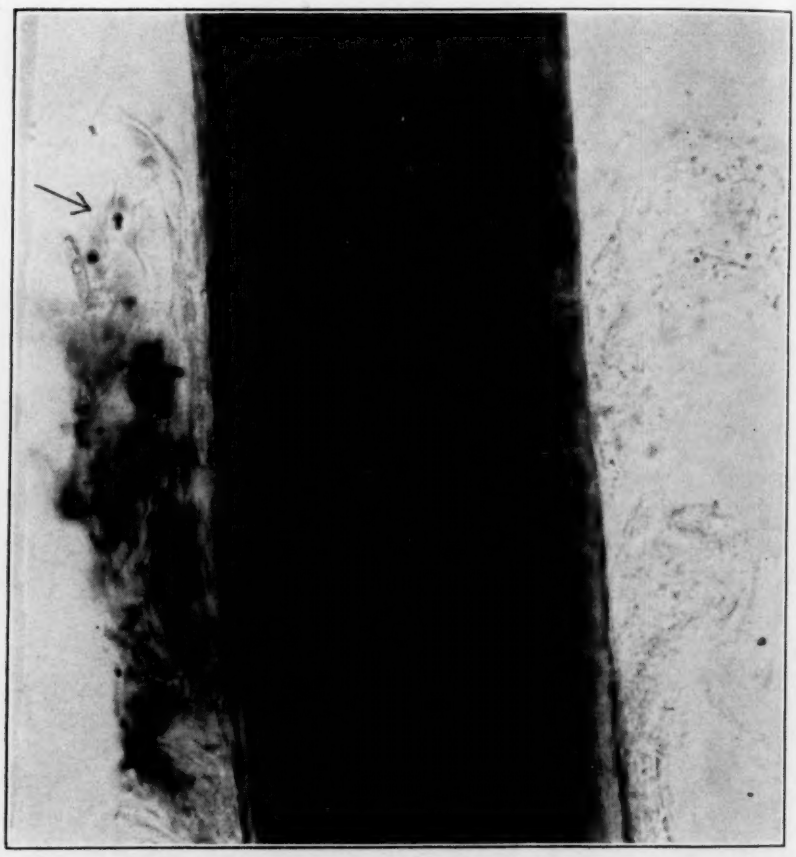

Fig. 5.—A hair removed from the eyelid of a patient with blepharitis marginalis and seborrheic eczema of the scalp. Organisms are seen in the scale about the hair. Methylene blue stain.

P. ovale was isolated and grown on 3 occasions. Hairs pulled out of the eyelids of patients suffering with blepharitis marginalis showed the organism about the hair of nearly every patient whose scales had shown it. It was usually present along that portion of the hair which occupied the upper part of the follicle, as well as in the scales that clung to the hair (fig. 5).

In addition, scales were taken from the eyelids of six patients and inoculated on an excoriation on the chest in the same manner as was done with scales from the scalp. Two positive reactions, consisting of scaliness, slight erythema and subsequent turning brown, were obtained. The other patients gave negative reactions, as did the controls (table 1).

Five rabbits were inoculated with P. ovale, the organism being rubbed along the margins of one eyelid. No reactions were noted.

COMMENT

Further observations of the relation of seborrheic eczema to P. ovale have been presented. In most instances our previous findings have been substantiated. The most significant and convincing studies, though the hardest to control, were those in which the scalp was inoculated with the whole culture of the organism. When one observes a scalp clinically free from seborrheic eczema, inoculates it with P. ovale and then in a few weeks finds numerous scales, itching and occasionally even excoriations, the relation of this organism to the disease is evident. Incidentally, these patients did not refrain from washing their scalps at the usual time or change their soaps. They did refrain from any beauty treatments, such as wave sets. The results of this series of 26 tests, with 69 per cent reactions definitely positive and another 20 per cent doubtfully so, are most significant.

The results of intradermal tests with pityrosporin were less significant, as the reactions were mild. No definite relation between any reaction noted locally and the presence or absence of seborrheic eczema elsewhere on the body was noted.

The series of patients with blepharitis marginalis, in which P. ovale was found in the scales and on the hairs of the eyelids, gave further evidence that this disease in many cases is just another manifestation of seborrheic eczema. It has been assumed by many ophthalmologists that blepharitis marginalis, especially the squamous type, is seborrheic eczema of the margins of the lids. The finding of numerous organisms in material from many patients with marginal blepharitis added further evidence of the possible relation of P. ovale to seborrheic eczema in general.

SUMMARY

A further series of inoculations with P. ovale is presented. Inoculation of the chest gave significant reactions in many instances. Inoculation of whole culture of P. ovale into the intact skin of the scalp gave a series of important and significant results, in that clinical seborrheic eczema of the scaly type was often reproduced.

A further series of intradermal tests with pityrosporin was carried out, with results similar to those reported previously. The reactions

were always mild and could not be correlated with the presence or absence of seborrheic eczema.

A series of patients with scaly blepharitis marginalis was studied. P. ovale was found in the scales of 21 of 24 patients examined. Examination of hairs from the eyelids of some of these patients showed the organism along the upper hair shaft as well as in the scales that clung to the hair.

ABSTRACT OF DISCUSSION

Dr. Richard S. Weiss, St. Louis: The etiology of the seborrheic dermatoses has always been of great interest to workers in the dermatologic field. Many years ago Unna and Engman Sr. grew the organism then known as the bottle bacillus or the spore of Malassez, but they were successful in making only one or two subcultures.

Sabouraud in 1902 expressed the thought that the organism was an involution form of the "gray coccus."

Castellani in 1925 apparently had grown the organism, but his description was insufficient for identification.

Templeton in 1926 seemed to have cultured the organism but to have succeeded in subculturing it only once. It was successfully grown by Acton and Panja in 1927. The growths obtained by MacLeod and Dowling in 1928 were doubtful.

In 1933 Ota and Huang reported successful cultures which continued to be viable for as long as four months.

In 1935 Moore and Kile reported successful culture and subculture, and Moore in the same year published a complete and detailed description of the organism.

In 1936 Moore, Kile, Engman Jr. and Engman Sr. reported further suggestive studies with human and animal subjects, and now Kile and Engman Sr. are reporting the results of human inoculations and the finding of the organism in blepharitis.

The great difficulty lies in establishing the pathogenicity of the organism. Its ubiquitous occurrence makes this hard, but it seems to me that so far it has been established that the organism is found in most seborrheic conditions; that it can be successfully cultured from many patients with seborrheic diseases, including blepharitis; that it can be found in sections and scales from seborrheic lesions, and that seborrheic eczema has apparently been produced by inoculation of the organisms.

Further studies are of course necessary, and these findings must be corroborated. The authors make no claim that the etiologic relationship of P. ovale to seborrheic conditions in general is absolutely proved, but I agree with them that their findings are suggestive.

Dr. Morris Moore, St. Louis: I do not wish to appear too dogmatic with regard to this, an almost universal disease, yet on the other hand, in the face of the suggestive research experience presented here and the almost positive results shown, I do not wish my enthusiasm to be lessened.

The earlier published work of my associates and me presented extremely suggestive results. I should like to show now a few slides that I showed at the meeting of the American Dermatological Association in 1935, in support of our contention that P. ovale, a small yeastlike organism, plays a suggestive rôle in seborrheic eczema.

Before I show the slides I should like to say that seborrheic eczema, or seborrheic dermatitis, in view of the evidence that we present here, is probably a misnomer, and I should like to have suggestions for a better name for the disease.

In the acute, rapidly spreading infection the organism is small, bottle-like, varying in size from 2 to 4 microns, the so-called Flaschen-Bacillus of Unna, or the bottle bacillus, as it was known later. In chronic lesions which have been treated with something harmful to the growth of the organism, there are larger, thick-walled cells, indicative of an unfavorable condition and known as resting cells, together with the smaller, typical bottle-shaped cells.

When the organism was first grown it took on this appearance. The thick-walled cells seen here are due primarily to some constituents of the medium, beerwort agar, made up of maltose, beerwort and glycerin, which usually produced much larger cells.

Here are some of the subcultures of the organisms in different mediums. Here is a culture in beerwort agar, here one in malt extract and here a poor growth on cornmeal agar. Here is a growth in Sabouraud's maltose agar, here one in brain veal agar and here in glycerin agar the best growth of all, which is analogous to that found in the oil on the skin, where the organism flourishes most.

Seborrheic eczema in itself has no histologic features to differentiate it clearly from any other dermatitis. Of course, there is a huge amount of fat in the epidermis; the various characteristics of excoriation, hyperkeratosis, well marked at the mouth of the hair follicle, parakeratosis, acanthosis and in some cases an extension, and in others a flattening, of the interpapillary rete pegs as a result of the parasitic organism are seen. Also seen here are a perivascular infiltration of the lymph spaces, and intercellular and intracellular edema. This is all probably shown more clearly in the next slide. My associates and I have been able to see microscopic vesicles, which are suggestive of normal-appearing seborrheic eczema. These sections were taken from one of our experimentally inoculated subjects who clinically presented the complete picture of so-called seborrheic eczema.

Here is seen the mouth of the hair follicle and the follicle itself, with a huge amount of parakeratosis and extension of the rete pegs.

The marked histopathologic condition of the hair follicle, the result of the invasion of P. ovale, appears here. This is more marked in this oil immersion enlargement of that same follicle, which shows the invading organisms. The organism as it appears in the culture is a large cell; it becomes much larger owing to a better substratum to grow on. However, as it appears in the parasitic stage or as it becomes better adapted to its parasitic method of life (it is changed from saprophytism to parasitism), the morphologic characteristics of the organism change from those of a large saprophytic cell to those of a small parasitic, highly invasive cell.

We do not claim that this organism produces the disease directly, but I think the evidence we present is extremely suggestive.

Dr. H. J. Templeton, Oakland, Calif.: In 1924, while working in the clinic of Dr. Schamberg and later in that of Dr. Harry Alderson, I succeeded in growing this organism, P. ovale, in pure culture. This was accomplished by inoculating the scales from the scalp on beerwort agar and on beerwort agar treated with a small amount of oleic acid. Unfortunately, I was not at that time successful in carrying the growth beyond the first subculture. My associates and I had no difficulty in isolating this organism on direct microscopic examination

from practically all scalps showing any seborrhea or scaliness, but unfortunately we were also able to recognize it in direct examination of most so-called normal scalps. In spite of that discrepancy, I have always felt, along with Dr. Kile, that this organism does have something to do with seborrheic eczema.

I have felt that certain of the seborrheic dermatitides of the trunk, such as the follicular and the circinate seborrheids, which are ids in the morphologic sense of the term, are also ids in the biologic sense, that is, that they express the reaction of a sensitized skin, the shock organ, to a primary focus of the allergen in the scalp.

If this is correct, intradermal desensitization by means of the antigen which the essayists have mentioned might be of some value in treating the id of the seborrheic group. I should like to hear the essayists' reaction to this idea.

Dr. Marion B. Sulzberger, New York: I should like to compliment the essayists on their report of the successful growth of a fungus which has been shown to be difficult to culture.

I believe that a great deal more work must be done before evidence can be accepted that this organism produces seborrheic eczema. I have seen no histologic or clinical pictures presented which demonstrate the production of a typical cutaneous disease of long duration without spontaneous healing or of lesions characteristic of seborrheic eczema experimentally produced by P. ovale in human inoculations. One can take many contaminants of the skin, many saprophytic fungi, such as mucors, aspergilli and penicillia, and many other micro-organisms which one finds on the cutaneous surface and by scarifying an area of normal skin and rubbing some culture into the injured surface produce lesions of the type which Drs. Engman and Kile have shown on the scalp, and which they produced by inoculation with P. ovale.

I believe that new or convincing evidence that P. ovale actually causes seborrheic eczema is still completely lacking, and I am pleased to hear that the essayists are of the same general opinion.

Dr. Roy L. Kile, St. Louis: In answer to Dr. Templeton, I may say that in the circinate lesions of seborrheic eczema we have found large numbers of the organism.

I agree with Dr. Sulzberger, as I have previously stated, that this work needs confirmation and that no absolute proof of the pathogenicity of this organism is available at the present time, but as Dr. Weiss stated, the evidence is suggestive. All we have attempted to do is to present the observations that we have accumulated. We have drawn no conclusions, for we would rather leave that to the members. It is exceedingly hard to prove the pathogenicity of an organism of this sort. We have tried inoculating other organisms and P. ovale side by side, and, as Dr. Sulzberger says, occasionally we could see some scaliness from other organisms. It was entirely different from that produced in the positive inoculations with P. ovale. Control tests were made whenever possible.

Although some of the evidence is alluring, we have drawn no conclusions and merely present the results of our observations.

RELAPSE IN LUPUS ERYTHEMATOSUS AFTER TREATMENT WITH SODIUM GOLD THIOSULFATE

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DURHAM, N. C.
AND
JOHN H. STOKES, M.D.
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In the ten years since Schamberg and Wright [1] introduced sodium gold thiosulfate into this country for the treatment of lupus erythematosus, it has been interesting to observe the various reports concerning its efficacy. The earlier reports were extremely favorable, as enthusiasts hailed it as a perfect remedy. Later, as reports of its toxic and occasional serious reactions appeared, it was damned by many as a dangerous drug. In the past few years, however, it seems to be assuming its rightful position as a useful adjunct and possibly the best single remedy in the treatment of lupus erythematosus.

In spite of the excellent results obtained by many, in our hands relapses and recurrences were frequent. A survey of cases observed in the dermatologic clinic of the Hospital of the University of Pennsylvania and in the practice of one of us (J. H. S.) disclosed 31 in which apparently adequate treatment with sodium gold thiosulfate had been given and which had been followed over a sufficiently long period to justify drawing certain conclusions.

A review of the literature reveals a plethora of reports relative to the use and the value of sodium gold thiosulfate. Only such articles as may be concerned with this communication will be cited. Towle's [2] review of 420 cases, of which he found that good results were obtained in 93 per cent, and the ten year evaluation by Wright [3] summarize well the general opinion as to its therapeutic value. Driver and Weller [4]

1. Schamberg, J. F., and Wright, C. S.: The Use of Gold and Sodium Thiosulphate in the Treatment of Lupus Erythematosus, Arch. Dermat. & Syph. **15**:119 (Feb.) 1927.

2. Towle, H. P.: The Present Status of Gold Therapy, New England J. Med. **204**:487 (March 5) 1931.

3. Wright, C. S.: Ten Years' Experience in the Treatment of Lupus Erythematosus with Gold Compounds, Arch. Dermat. & Syph. **33**:413 (March) 1936.

4. Driver, J. R., and Weller, J. N.: Untoward Results from the Use of Gold Compounds, Arch. Dermat. & Syph. **23**:87 (Jan.) 1931.

and Throne, Kingsbury and Meyers [5] have admirably covered the unfavorable reactions to sodium gold thiosulfate. Gold compounds have been held inferior to bismuth preparations by many—notably Smith,[6] who held that gold is definitely inferior to bismuth, is more toxic, aggravates existing tuberculosis, causes severe focal reactions, requires a more elaborate injecting technic and is more expensive. Wise and Sulzberger [7] stated that gold salts may be used in the treatment of lupus erythematosus, provided bismuth preparations have failed, but in their opinion should not be used as a first measure.

As early as 1929, however, two years after the introduction of sodium gold thiosulfate, Ormsby [8] called attention to the many recurrences in cases in which brilliant results had been obtained. Goeckerman [9] said that he never obtained cure in more than 50 per cent of cases of erythematous lupus with sodium gold thiosulfate, and in cases in which the response to treatment was favorable many relapses occurred. Lashinsky [10] expressed the belief that if there is no improvement after twenty injections, treatment will be of no avail. Rutledge [11] found about 10 per cent of his patients suffered relapse, and others often required three or four courses for cure. Haxthausen [12] found that after recurrence or relapse the disease is much more resistant to treatment than before. Diasio [13] found many recurrences after the use of sodium gold thiosulfate, especially in warm weather.

We proceed now to the analysis of the 31 consecutive and unselected cases in our series. Of the 31 cases traced, in 22, or 74 per cent, there were relapses. Each patient had from one to four relapses. The ages of the patients varied from 16 to 61 years, and the observed relapses had no relation to age. It was evident, however, that patients whose

5. Throne, B.; Kingsbury, J., and Meyers, C. N.: Unusual Clinical Manifestations Following Intravenous Administration of Gold Compounds, Arch. Dermat. & Syph. **25**:494 (March) 1932.

6. Smith, A. G.: Gold and Bismuth in the Treatment of Lupus Erythematosus, Brit. J. Dermat. **46**:399 (Oct.) 1934.

7. Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1935, p. 452.

8. Ormsby, O., in discussion on Stillians, A. W.: Lupus Erythematosus, Arch. Dermat. & Syph. **20**:382 (Sept.) 1929.

9. Goeckerman, W. H., in discussion on Stillians, A. W.: Lupus Erythematosus, Arch. Dermat. & Syph. **20**:382 (Sept.) 1929.

10. Lashinsky, I., in discussion on Spinner, G. J.: Lupus Erythematosus, Arch. Dermat. & Syph. **25**:1176 (June) 1932.

11. Rutledge, W. U.: Lupus Erythematosus: Treatment with Gold Preparations, Arch. Dermat. & Syph. **23**:874 (May) 1931.

12. Haxthausen, H.: Treatment of Lupus Erythematosus by Intravenous Injections of Gold Chloride, Arch. Dermat. & Syph. **22**:77 (July) 1930.

13. Diasio, F. A.: Treatment of Lupus Erythematosus, with Special Reference to Value of Gold and Bismuth Compounds, M. J. & Rec. **137**:375 (May 3) 1933.

involvement was extensive, with many lesions, experienced relapse more often (82 per cent) than those patients with mild involvement or few lesions (57 per cent). Seventeen of forty relapses observed (42 per cent) were definitely related to exposure to sunlight, and 85 per cent of all relapses occurred during the spring or the summer. Relapses occurred without relation to any interval of time, patients who had had lupus erythematosus only a few months experiencing relapse as often as patients who had had the disease for as long as fifteen years. Relapses occurred after apparent cure without any recognizable relation to time. Some patients suffered relapse within one month after "cure," while others remained entirely free from lesions for as long as thirty-six months. Sex and race played no role in relapses. No relation was observed to the total or the average dose of sodium gold thiosulfate, relapse occurring as frequently after a total dose of 7,700 mg. as after as little as 200 mg. and as frequently in patients receiving doses of from 3 to 35 mg. as in those receiving doses of from 50 to 200 mg.

Possible Explanatory Factors in Relapse

Total number of relapses	40
Total number occurring:	
in spring or summer	34
after exposure to sunlight	17
after nervous stress and strain	7
after roentgen irradiation to face for another disease	1
after mycotic flare-up	1
after intercurrent infection (influenza, pleurisy)	3
after alcoholic overindulgence	2
No data	9

Certain possible explanations for relapse were obtained from the histories. Twenty-three patients gave a history of previous oversusceptibility to sunburn. This proved to be significant, for 17, or 42 per cent, of the patients experiencing relapse gave a definite history of relapse following exposure to sunlight. Eighty-five per cent of the relapses (34 of 40) occurred during the spring or the summer, which suggests the influence of sunlight, though definite exposure could not be demonstrated in all cases. Nervous stress and strain undoubtedly played a part in causing certain of the relapses (7 patients), particularly among high-strung patients in private practice. In these patients relapse seemed to be associated with the appearance of the rosacea complex under stress. Two cases may perhaps in part illustrate this factor.

REPORT OF CASES

CASE 1.—A 37 year old white woman with lesions on her face and an associated rosacea was responding well to regular injections of 50 mg. of sodium gold thiosulfate. After loss of sleep and much worry over an impending break-up in the

family (all other factors remaining unchanged) a marked flare-up of her lupus erythematosus appeared.

CASE 2.—A 35 year old white woman with lesions over the nose and the cheek had experienced almost complete clearing of the condition but was still under regular treatment with 50 mg. doses of sodium gold thiosulfate. Relapse occurred after she was told that she must have a cesarean section. On a second occasion when the eruption was markedly improving she experienced a marked flare-up after a serious domestic crisis.

Intercurrent infections such as those observed by Stokes and Callaway [14] in other dermatoses seemed to play an important part in 3 cases of a type illustrated by the following case:

CASE 3.—A 24 year old white man with lesions on both cheeks was receiving sodium gold thiosulfate in 75 mg. doses. He was responding satisfactorily when, after his thirty-third injection, severe influenza developed. Concurrently he experienced an almost total relapse of his erythematous lupus, and his course was much less favorable after the relapse.

This is in agreement with the recorded observation of Haxthausen.[12]

A severe mycotic flare-up was a possible explanatory factor in another case:

CASE 4.—In a 55 year old white man with lesions on his cheeks, his lips and his ears, who was progressing favorably with regular injections of 75 mg. of sodium gold thiosulfate severe mycosis and mycotid dermatitis developed. These were followed in one week by the relapse of his lupus erythematosus.

Relapse followed alcoholic overindulgence in 2 cases and the receipt of 93 r of roentgen therapy to the face for mild dermatitis in 1 case.

Six patients who suffered relapse gave histories of familial allergy, and 5 of the patients stated that they were allergic. This represents 20 per cent of the patients in the series. A seborrheic background was noted in 25 of a group of 31 patients (80 per cent) observed, and 2 patients had concomitant rosacea. There has seemed to be a rather close relation between resistant erythematosus lupus and seborrheic processes, especially in the scalp, in our experience.

SUMMARY

Seventy-four per cent of 31 patients with lupus erythematosus suffered relapses after treatment with sodium gold thiosulfate.

Certain possible explanatory factors in relapse are discussed.

14. Stokes, J. H., and Callaway, J. Lamar: Pyogenic Relapse and Sensitiveness to Light in Certain Dermatoses: Influence of a Factor of Intercurrent Infection, Arch. Dermat. & Syph. **36**:976 (Nov.) 1937.

CUTANEOUS HAZARDS IN THE CITRUS FRUIT INDUSTRY

BRIEF HISTORY OF CITRUS FRUIT IN FLORIDA AND IN CALIFORNIA

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The value of citrus fruit as a food and as a medicinal agent has been known for many centuries. There are Chinese and Japanese records available from as early as the seventeenth century which extol the medicinal value of citrus fruits. Their value as antiscorbutic agents has been known since the seventeenth century, and within recent years they have been found to be sources of vitamins A, B and C and of comparatively large quantities of calcium.

The orange is not a native of the United States. It was introduced by the Spaniards first into Florida and later into California. The Spaniards themselves obtained the fruit from the Portuguese, who had previously brought it from China. The first variety introduced into the United States ripened in December, January and February, but through intensive cultivation different varieties of oranges are now grown which ripen throughout practically all the year.

The early varieties produced in Florida, such as the Parson Brown, ripen between October and December. The midseason varieties, such as the pineapple and the seedling, ripen between December and March, and the Florida valencia orange matures between March and June.

In California, the valencia orange matures between April and November, and the navel orange matures in the fall and winter, being picked between November and May. The navel orange industry began in California from two small trees sent from the United States Department of Agriculture in Washington, D. C., to Mrs. Eliza C. Tibbetts, of Riverside, Calif., in 1873. These trees were sent to Washington from

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This report is based on examinations and studies of processes in five large citrus fruit groves, twenty citrus fruit packing houses, sixteen citrus fruit canneries, four fertilizer plants and two insecticide manufacturing plants. In addition, consultations were held with representatives of the United States Department of Agriculture and with chemists, physiologists and other officials interested in the production, handling and marketing of citrus fruit.

Patch tests with chemicals used in treating oranges, with citrus peel and with citrus oils were performed on forty-six volunteers.

Bahia, Brazil, where it is thought that they originated as a bud sport of the selecta Portuguese orange.

The growing of oranges begins with the planting of the seed for rootstocks.[1] The principal rootstocks on which oranges are budded are those of the sour orange (Citrus aurantium Linn), which is said to be the first member of the citrus family to be introduced into Florida; the rough lemon (Citrus limonia Osbeck); the sweet orange (Citrus sinensis Osbeck); the trifoliate orange (Poncirus trifoliata), and the grapefruit (Citrus paradisi). The rootstock is selected according to the kind of soil in which it is to be placed, and the variety of orange desired to be grown is budded on it after the seedling is about 2 years old. The fruit produced on the budded tree will be the same as that produced by the tree from which the bud was taken, no matter what kind of rootstock is used, while the tree will have the rugged root system of the selected rootstock. Young trees which have been budded are allowed to remain in the nursery for at least a year before they are planted in groves. From sixty to one hundred trees are planted on an acre (4,050 square meters) of ground, the number depending on the kind of soil, and the tree begins to bear fruit when it is about 6 years old.

FREQUENCY OF CUTANEOUS INJURIES IN THE CITRUS FRUIT INDUSTRY AND DESCRIPTION OF THE INJURY

The records of an insurance company which carries the risks of growers and packers of citrus fruits were examined for a period covering the year 1935-1936, and among a total of 3,184 accidents and injuries there were found to be 261 cutaneous injuries and rashes. Among this number a large majority (203) were due to pricks by thorns. Twenty-six, or less than 1 per cent of the total number of injuries, were classified as dermatitis, and of this number, 19 were due to lemons.

In order that crops of good fruit may be produced citrus groves must be fertilized, and citrus trees must be treated for the killing off of insects and other parasites.

Cutaneous hazards in the citrus fruit industry begin with the fertilizers used on the soil. In the fertilizer manufacturing plants visited during this study it was found that various mixtures of nitrates, lime, sulfur, potassium carbonate, phosphates, cyanamide, bone meal, fish meal, castor pumice, blood, animal tankage, peet and citrus peel are sold as fertilizers for citrus groves. The mixtures of these fertilizers differ according to the kind of soil on which they are to be used and the variety of citrus fruit desired to be grown. The men working in the fertilizer manufacturing plants stated that dermatitis occurs among

1. Camp, A. F.: Citrus Propagation, Bulletin 227, University of Florida, Agricultural Experiment Station, April 1931.

them from the dust of many of these fertilizers. The principal ones named as irritants were calcium nitrate, lime, potassium carbonate, cyanamide and bone meal. One man who was engaged in mixing cyanamide with ground citrus peel and peet stated that on two occasions when he had indulged in alcoholic beverages after work a swelling had developed on the face and the eyes, accompanied with dizziness and nausea, typical symptoms of cyanamide poisoning. He also had a dermatitis of the legs at the point where his trousers, which were saturated with cyanamide, touched the skin.

Dermatitis and burns in the fertilizer plants are not as common as one would expect from the nature of the chemicals handled, because the workers are heavily clothed to prevent dust from penetrating to the skin; but ulcerations of the nasal septum were found in a considerable percentage of the workers examined. These lesions occur because the men do not like to wear respirators and because the nitrates, the lime and the cyanamide when inhaled cause ulcerations of the nasal septum.

Dermatitis may at times develop among the workers in the groves who spread the fertilizers, and they may suffer from chemical burns if they are not properly protected against the irritating fertilizers.

Insecticides in the form of dusts, sprays and gas are used on the trees several times during the year. Highly refined sulfonated mineral oils, alone or in various combinations, such as oil-nicotine-lime-sulfur, oil-nicotine-zinc and sulfur-oil-zinc, are commonly used as insecticide sprays.[1a] Watery solutions or suspensions of copper sulfate, Bordeaux mixture, lime, nicotine, sulfur and derris are also used as insecticides for various forms of "rot." Lime and sulfur are used in the form of dust. The use of arsenic is rigidly prohibited on orange trees, but it is sometimes surreptitiously used on grapefruit trees. When arsenic is sprayed on the leaves of citrus trees, it is said to increase the respiratory rate and decrease the acid content of the juice, thus raising the ratio of sugar to acid. It is also said that arsenic so sprayed on the leaves does not appear in the juice.

Since the discoveries that fluorine causes mottled enamel and that selenium causes poisoning, their use has been prohibited on citrus trees.

The trees are at times fumigated with hydrocyanic acid gas. When this is done, each tree is covered with a canvas tent, and the gas is allowed to enter the tent from a cylinder containing the liquefied gas. Cases of poisoning and dermatitis have been known to occur because of this procedure.

1a. Thompson, W. L.: Lime-Sulfur Sprays for Combined Control of Purple Scale and Rust Mites, Bulletin 282, University of Florida, Agricultural Experiment Station, July 1935.

Spraying and dusting are done by machines, through a hose and nozzle with an air pressure attachment.

No dermatitis attributed to insecticides was observed during the course of this study, but the condition was said by owners of groves to occur occasionally among some hypersensitive sprayers when they are not properly protected by goggles and clothing.

Groves located in climates where freezing temperatures sometimes occur have scattered through them heaters, which are lighted when the thermometer nears or reaches the freezing point. Early forms of heaters created huge volumes of dense smoke as well as heat, and this smoke was deposited on the trees and the fruit. Hence, the heating operation was known as smudging. More modern heaters give more heat and less smoke. No dermatitis was attributed to smudging.

It was found that when the fruit is picked from the trees if the skin of the orange is injured it forms an entrance for decay. Because of this, fruit pickers are required to wear gloves, so that the finger-nails cannot injure the peel, and to carry a bag in which they deposit the fruit as it is picked from the tree (fig. 1). This bag is so constructed that the bottom of it can be opened and the contents emptied into a box without injury to the fruit. The fruit is carefully clipped, not pulled, from the stem, so that neither the peel nor the "button" on the stem end is cut. The stem is not left long, because it might puncture other fruit with which it comes in contact. Specially constructed boxes with smooth inner surfaces, to protect the fruit from injury, are used in hauling the fruit from the grove to the packing house.

The cotton gloves usually worn by the pickers to protect the fruit from injury offer little protection to the skin of the workers against the long, sharp and tough thorns which are characteristic of many varieties of citrus trees. These thorns often penetrate deeply, and wounds from them are common among pickers of citrus fruit. These wounds at times become infected and cause the workers to lose considerable time from work. Among 180 cases in which this occurred the average loss of time per worker was four days. When leather gloves and wrist bands are used, injuries to the skin from thorns are materially reduced. The face, the eyes and the arms are at times injured by thorns.

Wounds from splinters of wood on the outer sides of boxes often occur, because such careful attention is not given to smoothing the outer surfaces.

TREATMENT OF ORANGES

The fruit is transported from the groves to the packing houses, where it undergoes various forms of treatment before shipment. A description of all the processes through which an orange goes before it is ready to be shipped follows. All oranges do not go through all the processes, some of them being only washed, dried and packed before shipment.

Precoloring.—If the oranges are green they are placed in chambers, which are closed and made air tight, and exposed to ethylene for from twenty-four to ninety-six hours. This hastens the disappearance of the green chlorophyll from the peel and allows the natural coloring matters of the peel (carotene and xanthophyll) to show through and give the fruit a yellow color. This process, called "precoloring," was discovered when kerosene stoves were used in packing sheds in order to guard against the danger of injury by frost to fruit stored there. It was found

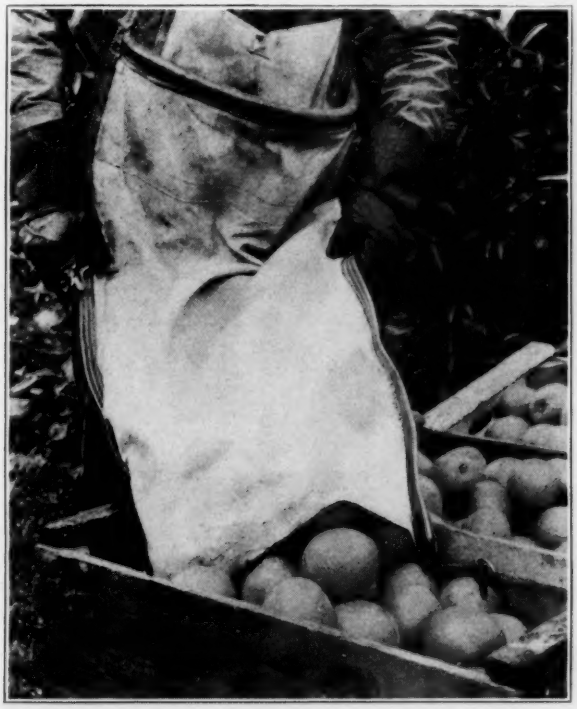

Fig. 1.—Orange picker wearing leather gauntlets to protect the hands from thorns and the fruit from bruises. The bottom of the sack unfastens to prevent bruising of fruit. The rough exterior of the box constitutes splinter hazard.

that fruit exposed to the smoke from these stoves lost whatever green was in the peel. With further research the present ethylene precoloring process was developed, but in some packing houses the smoke from kerosene stoves is still used for precoloring. The usual length of time during which fruit is subjected to the gas does not adversely affect the eating qualities, but too long exposure to ethylene has a deleterious effect on the flavor of the orange and hastens the process of decay.

Some packing houses in California expose the oranges to nitrogen trichloride gas for six hours, in order to kill fungous growths before precoloring the fruit. If the oranges are to be kept in storage for any length of time before shipment, they may be again exposed to the action of this gas, and sometimes the gas is released into the railroad cars used in shipping the fruit. No dermatitis has been attributed to exposure to ethylene or nitrogen trichloride.

After being precolored the fruit is placed on traveling belts which first carry it into a cleansing solution of sodium borate or a strong alkaline soap, which may contain trisodium phosphate or soda ash

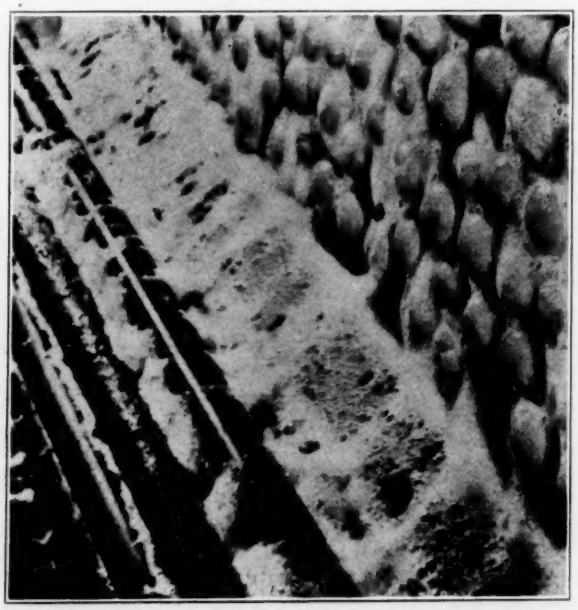

Fig. 2.—Oranges being automatically washed in an alkaline soap solution to remove "smudge" and insecticides.

(fig. 2). The fruit is automatically scrubbed by revolving brushes submerged in the tanks. This not only cleans off the dirt, the insecticides and the smudge, but tends to kill fungous growths. The belt carries the fruit from this bath into a rinse of clean water, which removes the excess of the washing solution (fig. 3), and then, if the fruit is not of the golden yellow, which the public is accustomed to associate with ripe oranges, the fruit is carried into the color or dye tank.

Why Oranges Are Dyed: Oranges are often mature before the peel turns yellow. Oranges of some varieties may contain the legal ratio of solids to acid (eight to one) when their peel is green, and the valencia orange will turn green again after it has already been yellow if it is

allowed to remain on the tree. The yellow color of an orange varies according to the soil in which the tree grows, the kind of fertilizer used, the amount of exposure to the sun while the fruit is on the tree and the variety of rootstock. The consumer has not been educated to the fact that the color of the peel is not a true indication of the maturity of the fruit and will not buy fruit which is not of a typical orange, even though it may be juicy and have a better than legal ration of sugar to acid. For this reason it is desirable to have oranges the color which the public associates with ripe oranges. Some oranges when treated with

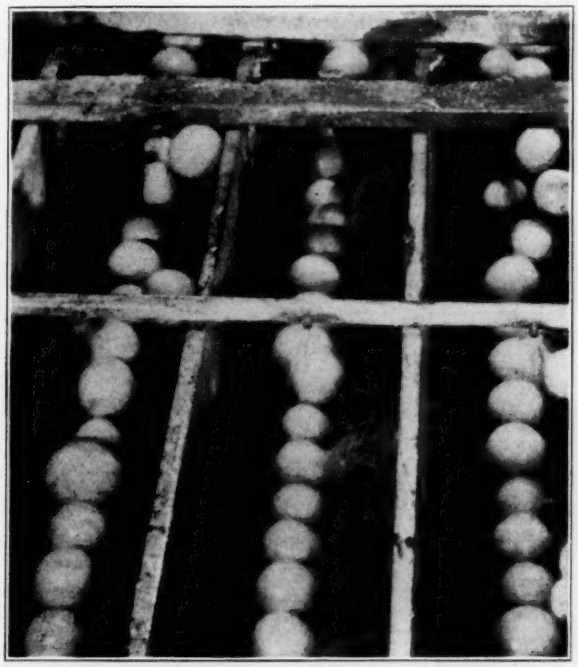

Fig. 3.—Automatic washing and scrubbing of oranges with water to remove excess of alkaline soap solution used for cleaning off dirt and insecticides. The same method is used for removing excess dye.

ethylene will attain this color, but others will be only a pale yellow. It is because of this that oranges are dyed.

California oranges naturally have the golden yellow color associated with mature fruit, and therefore the dyeing of oranges is not practiced in California. In Florida, where dyeing of oranges is practiced on a large scale, the Florida Citrus Fruit Commission requires that all fruit before being dyed must have a minimum of eight parts of solid matter in the juice to one part of citric acid, that dyeing should not be used to cover defects in the orange, and that all oranges to which dye is applied must be stamped "color added."

Method of Dyeing: In the year 1933, when the practice of dyeing oranges was begun, a number of different dyes were used by various packers. With many of these dyes the full color would not develop until long after the fruit had been dyed. With others the color faded on exposure to sunlight. This resulted in the shipping out of Florida of fruit which varied in color from tomato red to light yellow and prejudiced the buying public against Florida oranges. To overcome these conditions the Florida Citrus Fruit Commission now requires that only dyes with which the full color will develop within thirty minutes after dyeing shall be used on oranges and that this color must conform to a standard color scale, which varies with the season. This law does not apply to oranges which have been treated by the gaseous hydrocarbons and not dyed.

The majority of oranges shipped out of Florida have had color added. A small percentage of the crop, especially in midseason, may be only washed, dried, waxed, graded and sized.

The dyeing solution may consist of one of three dyes, two of which are sanctioned by the United States Food and Drug Commission as food dyes, and for the third of which sanction is pending. The first of these dyes is known as oil yellow OB, no. 61 in the Color Index, and has a chemical composition of ortho-toluene-azo-beta-naphthylamine; the second, oil yellow AB, no. 22 in the Color Index, has a chemical composition of benzene-azo-beta-naphthyl-amine; the third is said by the inventors to be ortho-toluene-azo-beta-naphthol. It is not listed in the Color Index. These different dyes are dissolved in various solutions: Oil yellow OB and oil yellow AB are used together and are dissolved in sulfonated oil. They are used in combination because one tends to fade in the sunlight while the other assumes a deeper color on standing, so that the action of the one tends to neutralize the action of the other. Ortho-toluneneazobetanaphthol is dissolved in a specially prepared soap solution. The amounts of dyes in these solutions vary from 0.06 to 0.2 per cent. In some packing plants the oranges are submerged in a warm solution of the dye; in some plants the dye is sprayed on the fruit; in others the dye is simply brushed on in conjunction with the wax while the oranges are being polished. When cold dyeing is done, the solvent used is a mixture of perchlorethylene, cyclohexanol and a soap solution and is usually put on in the form of a spray.

Waxing.—After the fruit is dyed, it is washed with water to remove the excess dye (unless the dye is brushed on with the wax), and then the wax is applied over the dye. Waxing is done either by submerging the fruit in an emulsion consisting of 10 per cent carnauba wax and 90 per cent paraffin wax, emulsified with the addition of triethanolamine, soap, shellac and water, or by spraying on a melted mixture of carnauba

wax [2] and paraffin. In some instances the fruit is simply brushed with paraffin. After the oranges have been coated with wax they pass in turn through a drier, over polishing brushes, by the graders, who place the oranges of different grades on different belts, and to automatic stamping and sizing machines. Oranges of different sizes are placed in different bins, are wrapped by hand in paper and are then packed in boxes, which are then nailed shut, ready for shipment.

As stated before, all oranges do not receive this complete treatment. Some are only washed, waxed and polished before being graded and packed. All dyed oranges, however, are waxed, so that the dye on the peel is always covered by a layer of wax.

Why Citrus Fruit Is Waxed: When citrus fruit comes off the tree it has a coating of natural wax on the peel, which serves to keep the fruit from rapid dehydration. The strong alkaline solutions used in washing the citrus fruit remove this natural wax. The coating of artificial wax is applied in order to replace this natural wax and to enable the brushes to put a better polish on the fruit. While a thin coating of wax slows down the natural respiration of the fruit and thus helps to preserve it, a thick coating may completely stop the natural respiration and hasten decay by favoring deleterious chemical changes and the growth of anaerobic bacteria.

In some packing houses, before the fruit is packed it is examined with a fluoroscope for soft areas in the pulp. When such soft areas are found, the fruit is rejected as imperfect.

TREATMENT OF OTHER CITRUS FRUIT

Grapefruit is given the same treatment as oranges, except that no dye is used.

Lemons are picked by size rather than by color. In fact, the best grade lemons are picked green. The picker carries a ring in his left hand, which he fits over the fruit. If the lemon passes through the ring, it is left on the tree. The fruit too large to pass through the ring is picked, including both the green and the yellow fruit. At the packing house the green fruit is separated from the yellow and after being washed is placed in storage rooms to ripen or "cure." The temperature of these rooms is maintained at about 55 F. and the humidity at 90 per cent. In "curing," the skin of the green lemon finally turns yellow. This may take weeks or even months. Lemons yellowed on the tree must be shipped to market quickly; otherwise they will spoil. When lemons come from the grove they are washed in an alkaline solution,

2. Carnauba wax is a yellowish, brittle substance extracted from the Brazilian palm (Copernicia cerifera), on the leaves of which it forms a deposit. The wax is scraped off as a powder from the dried leaves and then refined and bleached.

rinsed in water and stored wet. In some houses an additional washing is given with a solution of copper sulfate and sodium borate.

Limes receive only a washing with water and are then stored in the same way as lemons.

Many of the packing houses visited were beautifully designed and decorated so as to be restful and healthful to the workers. Others were crude and offered a minimum of sanitary devices.

CAUSES OF DERMATITIS IN THE CITRUS FRUIT INDUSTRY

Dermatitis from the handling of citrus fruit has been reported by many observers. Eczema due to lemon peel was reported by Fanburg and Kaufman.[3] Mackay and Ireland[4] reported sore finger-tips and superficial ulceration caused by lemon juice and stated that paronychia was found among persons handling lemons, peaches, crystallized fruits and flour paste and that syrup played a chief part in its causation. Traub and his associates[5] reported two cases of dermatitis which they attributed to the dye on oranges. Sutherland-Campbell[6] reported dermatitis among workers with oranges. Kingery and Thienes[7] reported the occurrence among handlers of citrus fruit of mycotic paronychia and dermatitis. Mayers[8] mentioned dermatitis from citrus fruits, and Horner[9] reported dermatitis from oranges and lemons. Legge[10] reported dermatitis among handlers of citrus fruits.

In the present study no dermatitis was found to follow the use of ethylene or nitrogen trichloride gas in the treatment of citrus fruit. Dermatitis was found among those workers who were required to come in contact with the strong alkaline solutions used for washing dirt and fungi from the fruit. The large majority of packing plants are equipped in such a manner that the hands of the workers do not get into the

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3. Fanburg, S. J., and Kaufman, J. G.: Eczema Due to Lemon Peel, J. A. M. A. **97**:390 (Aug. 8) 1931.

4. Mackay, K., and Ireland, I.: An Investigation into the Fruit Industry, Health Bull., Australia **15**:481 (July-Sept.) 1928.

5. Traub, Eugene F.; Gordon, R. E., and Van Dyke, L. S.: Dermatitis from Dyed and Otherwise Treated Citrus Fruits, J. A. M. A. **108**:872 (March 13) 1937.

6. Sutherland-Campbell, H.: Paronychia: Attempt to Prove Etiologic Factor in Epidemic Among Orange Workers, Arch. Dermat. & Syph. **19**:235 (Feb.) 1929.

7. Kingery, L. B., and Thienes, C. H.: Mycotic Paronychia and Dermatitis, Arch. Dermat. & Syph. **11**:186 (Feb.) 1925.

8. Mayers, M. R.: Occupational Dermatitis Due to Handling Plants, Vegetables and Fruits, Industrial Bulletin, New York State Department of Labor, August 1932, vol. 2, p. 342.

9. Horner, S. G.: Dermatitis from Oranges and Lemons, Lancet **2**:961 (Oct. 31) 1931.

10. Legge, R. T.: Fungus Infections of the Skin of Industrial Workers, Am. J. Pub. Health **21**:648 (June) 1931.

washing solution, but in a few, especially those where lemons are packed, the strong alkaline solutions wet the hands of the workers who are required to pick imperfect fruit, which floats light, from the washing tanks. Graders handling lemons which are taken out of hot washing solutions often suffer from dermatitis of the wrists at the points where their cotton gloves end. Dermatitis on the face, the eyes and the ears of these workers is sometimes caused by the lemon oil which is carried off by the steam from the hot lemons and by that with which the fingers of their cotton gloves are soiled. No dermatitis was found among the mixers or handlers of the dyes used in coloring oranges, although at the time the examinations were made many of these workers had their skins stained with the dye. No dermatitis was found among the graders of oranges who handle them after they are dyed and waxed. Among the packers of oranges, however, there was found an occasional worker who stated that dermatitis developed if she worked without gloves. These workers attributed the dermatitis to the fact that when they work without gloves they sometimes break the peel of the oranges and the oil which exudes as a result irritates the skin. Some packers suffer from tenosynovitis of the wrists due to twisting the paper wrappers on the fruit. In a large number of the packing plants it is compulsory for all workers to wear cotton gloves, but this is done more to protect the fruit from finger-nail bruises than for the protection of the skin of the workers. Workers in packing plants who handle citrus fruits should wear rubber and not cotton gloves. The cotton gloves may become saturated with the oil from the citrus peel and thus expose the skin to the oil more than if gloves were not worn.

The oil in the peel of citrus fruit is contained in the few layers of oil cells on the surface of the peel. Citrus oils are exceedingly irritating to the skin and will produce positive reactions when used in patch tests on the normal skin, in less than an hour. Citrus oil [11] is made up of a number of fractions, of which a terpene called *d*-limonene ($C_{10}H_{16}$) constitutes about 90 per cent. The remaining 10 per cent consists, in orange oil, of small percentages of decyl aldehyde, formic, acetic, capric and caprilic acids, octyl alcohol and linalool. The characteristic flavor of oranges is due to decyl aldehyde. Lemon oil, in addition to the *d*-limonene, contains pinene, citral, terpinene and geraniol. The characteristic flavor of lemon is due to citral ($C_{10}H_{16}O$). Grapefruit oil resembles both orange oil and lemon oil and, in addition to about 90 per cent of *d*-limonene, contains octyl and decyl aldehydes, octyl alcohol, geraniol, cadinene, citral and methyl anthranilate.

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11. Nelson, E. K., and Mottern, H. H.: Florida Grapefruit Oil, Indust. & Engin. Chem. **26**:634 (June) 1934. Poore, H. D.: Analyses and Composition of California Lemon and Orange Oils, Technical Bulletin 241, United States Department of Agriculture, March 1932. Nelson, E. K.: Florida Tangerine Oil, Am. Perfumer & Essential Oil Rev., September 1934.

Canning of Citrus Fruits.—Citrus fruit is put up in cans as juice and as hearts. Grapefruit and oranges are brought to the canneries directly from the groves in bulk. If grapefruit is to be canned as juice, it is washed in water and automatically cut by machines; the juice is either automatically squeezed out by machines or reamed out by hand. When hand reaming is done, the hands of the reamers are saturated with the juice of the fruit as well as with the oil of the peel. Reamers often suffer from dermatitis, which manifests itself as an erythematous, papular, vesicular rash of the dorsa of the hands and the forearms (fig. 4). Paronychia occurs in reamers but less frequently than does dermatitis.

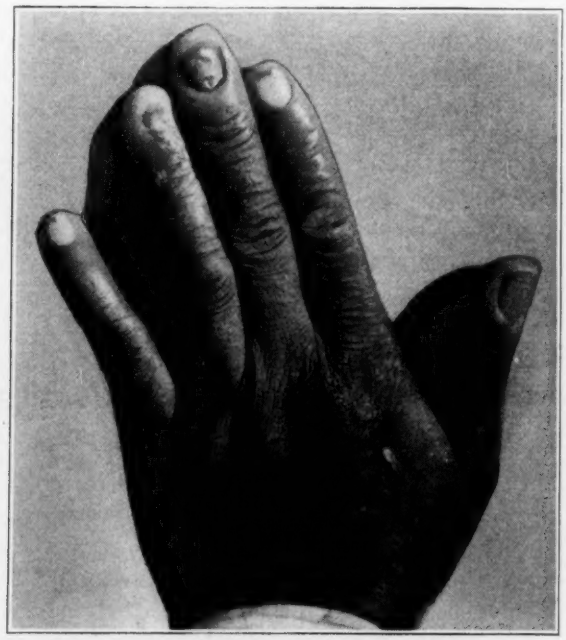

Fig. 4.—Paronychia and dermatitis in a grapefruit reamer.

When grapefruit is to be canned as hearts, it is first treated in most factories with hot water, which tends to loosen the peel. It is then peeled by hand, the peeling being started with a cut of the knife and finished with the knife and the fingers. The peelers often suffer from dermatitis and paronychia, and a large percentage of the peelers, especially in the early part of the season, are affected (fig. 5). The nails themselves are often eroded and eaten away, especially at the base. In most of the cases in which the involvement is mild, improvement occurs as the season advances and the patients are able to continue work, but

there have been cases in which the condition has been so severe that the worker had to leave the job, either of his own accord or by discharge.

After the fruit is peeled it is passed through a tank containing a hot solution of sodium carbonate, which removes the membrane from around the cells and those remnants of the rind which may have been left on by the peelers. After the fruit emerges from this treatment it is sprayed with water to wash off the excess alkali. It is then distributed to women, who remove the sections of the fruit, using a double-edged blunt knife, and place them in cans. A considerable percentage of these women, who are known as "sectioners," suffer from dermatitis and paronychia. Accidental cuts on their hands from thrusts of the knife become irritated from the juice of the fruit and require a long time to heal.

The workers in some grapefruit canning plants do what is known as "cold peeling," in which the fruit after being washed is peeled by

Fig. 5.—Paronychia in a grapefruit peeler.

women with sharp knives. The rest of the process is similar to that described previously. Dermatitis and paronychia occur even among the peelers and sectioners using this process of preparing grapefruit hearts.

Oranges that are hurt by frost or otherwise damaged are used for making orange juice, orange butter, orange marmalade and other orange products. When orange juice is made, the oranges are first washed and then sectioned, and the juice is squeezed from them either by hand reaming or by machine. When reaming is done by hand, dermatitis occurs among the hand reamers. When machines are employed to squeeze out the juice, some of the oil is also squeezed out from the peel. This mixture of juice and oil is then passed through a centrifuge, and the oil is separated. The juice is concentrated by evaporation; sugar and orange oil are added, and the product is sold to soda fountains and dairies. The peel from the orange is ground by machines and the oil extracted. While the operation is a mechanical one and there is little contact with the oil, those who do come in contact with it often suffer from dermatitis.

Citrus oils act as drying agents on the skin, extracting the fat and thus causing dermatitis.

Dermatitis and paronychia develop in workers who peel oranges to make orange butter from the pulp, but not as frequently as in peelers of grapefruit, because the oranges used for orange butter are usually dry and have comparatively little juice or oil in them.

Orange shredders, who feed orange peel to shredding machines in the process of making orange marmalade and orange preserves, are exposed to the oil from the peel and at times suffer from dermatitis.

Lemons are canned as juice. When reaming is done by hand the reamers suffer from dermatitis and paronychia. Lemon juice is said to be more irritating to the skin than either orange or grapefruit juice. It contains a higher percentage of citric acid.

Citric acid, lemon oil and citrus pectin are prepared from lemons by grinding the whole lemon in a machine and screening the juice thus obtained in order to separate the juice from the remnants of the pulp. The clear juice is then centrifugated, and the oil is separated. Citric acid is prepared by adding calcium hydroxide to the lemon juice and thus precipitating calcium citrate. The precipitate is filtered out and treated with dilute sulfuric acid, and citric acid crystallizes out of the solution when it is allowed to stand in a cold room.

A rash occurs in workers on the separators of lemon oil. Some of these workers seem to be more sensitive to the action of lemon oil than others.

Whatever is left of the citrus fruit after it passes through the canning operation is dried and used as citrus meal for feeding cattle. Where no facilities for preparing this meal are present, the refuse is sold in a moist state for fertilizer.

COMPOSITION OF CITRUS FRUIT JUICES

Grapefruit juice varies in specific gravity from 1.037 to 1.056. It constitutes from 46 to 56 per cent of the entire weight of the fruit. Citric acid comprises from 1.5 to 2 per cent and sugar from 4.7 to 9.5 per cent of the juice. The protein content varies from 0.36 to 0.56 per cent and the p_H from 3.36 to 3.74.

Orange juice varies in specific gravity from 1.046 to 1.057, and the juice constitutes from 44 to 59 per cent of the weight of the fruit. The citric acid content varies from 0.66 to 1.3 per cent, the sugar content from 7 to 10 per cent, the protein content from 0.36 to 0.74 per cent and the p_H from 3.6 to 3.9.

Lemon juice has a specific gravity of from 1.033 to 1.037, and the juice constitutes from 39 to 51 per cent of the weight of the fruit. Citric acid comprises from 4.5 to 6.7 per cent and sugar from 1 to 3 per cent of the juice. The p_H of lemon juice varies from 2.1 to 3.2.

Lime juice varies in specific gravity from 1.032 to 1.04 and constitutes from 50 to 62 per cent of the weight of the fruit. Citric acid comprises from 6 to 8 per cent and sugar from 0.83 to 1.74 per cent of the juice. The p_H varies from 2.3 to 3.2.

Traces of many of the constituents of the peel are found in citrus juice.

PREVENTION OF DERMATITIS IN CANNING PLANTS

Peelers, reamers, sectioners and those working around citrus oils should be required to wear rubber gloves reaching to the elbow to prevent the irritants contained in the juice and the peel from coming in contact with the skin. As much of the canning as possible should be done by machine. In plants where the juice is extracted entirely by machine there are less dermatitis and paronychia than in the plants where the process is less completely mechanized.

Workers in canning plants, in addition to the rubber gloves, should be required to wear working clothes supplied fresh daily and cleaned at the end of each shift. Machines, floors and walls should be cleaned daily, and workers in whom rashes develop in spite of these precautions should be transferred to some other occupation.

DERMATITIS AMONG CONSUMERS OF CITRUS FRUIT

Dermatitis occurs among attendants at soda fountains and workers in restaurants who squeeze the juice out of or prepare citrus fruit for consumption. A few persons are so allergic to citrus fruits that an inflammation develops on the lips and the skin around the lips and even generally after they eat citrus fruit. Cases of this kind were observed in the course of this study, but they are no more frequent than those of dermatitis following the eating of strawberries, tomatoes and fish and should not prejudice normal persons against eating citrus fruit.

PATCH TESTS WITH CITRUS OILS, PEELS, JUICE AND DYES

Patch tests were performed on thirty volunteers, in order to determine the irritating properties of citrus peels and oils. Five were tested with undyed orange peel, which was broken in such a way as to allow the orange oil to wet the skin, and the orange peel was then placed, oil cells down, on the portion of the skin which was wet with the orange oil. A piece of nonwaterproof cellophane was then placed over the orange peel, and a piece of adhesive plaster was used to hold the patch in place. After one-half hour there were severe reactions under all the five patches. The five patch tests in this experiment consisted of three pieces of orange peel from an undyed Florida orange and two pieces from an undyed California orange.

In order to determine whether the orange oil in the peel caused these reactions, twenty-five volunteers were given patch tests with orange peel prepared in the following manner: A California orange was taken from the tree and washed in plain water to remove the smudge. A punch was then forced against the peel down to the pulp, and the circular piece of peel was removed in such a way that the oil cells on the surface were not ruptured, as they are apt to be if the peel is bent when removed from the orange in the ordinary way. A circular hole smaller than the punched-out piece of orange peel was made in a piece of cellophane, and the cellophane was placed on the skin. The piece of punched-out orange peel was then placed over the hole in the cellophane in such a manner that the cut edges of the peel were kept from touching the skin by the interposition of the cellophane. This was done so that none of the oil from the cut edges of the peel could touch the skin. The whole was covered with a piece of adhesive tape and allowed to remain on for twenty-four hours. At the end of this time only one of the twenty-five subjects showed a positive reaction, and that was faint. These two experiments demonstrated that when positive reactions are obtained from patch tests with citrus peel, they are most likely due to citrus oil which has oozed out of accidentally ruptured oil cells. Great care must be taken in patching with citrus peel in order to avoid the breaking of these cells and the consequent exposure of the skin to citrus oils, because these citrus oils will irritate the normal skin and reactions from them do not indicate hypersensitivity.

Five volunteers were given patch tests with lemon peel prepared in the same manner and allowed to remain on for twenty-four hours. There were no reactions.

Five volunteers were given patch tests with lemon oil. There were five positive reactions in thirty minutes. Five volunteers were tested with orange oil, and there were five positive reactions in less than thirty minutes. Five volunteers were tested with *d*-limonene, and there were five positive reactions in less than thirty minutes. Five volunteers were tested with concentrated orange oil, which is prepared from orange oil by removing the *d*-limonene, and there were five positive reactions in sixty minutes. Five volunteers were tested with citral, the compound which gives the characteristic taste to lemons, and there were five positive reactions in twenty-four hours.

These experiments show that lemon oil, orange oil and *d*-limonene will produce positive reactions in less than thirty minutes when used in patch tests on the normal skin and that if the *d*-limonene is removed from these oils it takes a longer time for them to produce irritation. Therefore, *d*-limonene is the most active cutaneous irritant of citrus oils.

A series of experiments was performed to determine what percentage of citrus oils may be allowed to stay on the normal skin for

twenty-four hours without causing a reaction. Five volunteers were tested with mixtures of one part lemon oil and four parts liquid petrolatum and of one part lemon oil and nine parts liquid petrolatum. Five volunteers were tested with the same percentages of orange oil in liquid petrolatum. There were no reactions at the end of twenty-four hours. One of the volunteers submitted to patch tests with one part *d*-limonene and one part liquid petrolatum and with one part *d*-limonene and three parts liquid petrolatum. At the end of twenty-four hours there was a reaction under the patch consisting of half *d*-limonene but no reaction under the patch consisting of one-fourth *d*-limonene.

Five volunteers were tested with pure orange juice, pure lemon juice and pure grapefruit juice, and the patches were left on for twenty-four hours. When the patches were removed, there were no reactions, but the next day one of the subjects showed a delayed reaction to orange juice. It seems from this experiment that most skins will not react to pure orange juice, lemon juice or grapefruit juice if the juice is left on for twenty-four hours.

In order to test the irritating properties of the dyes used on oranges, patch tests were performed on sixteen volunteers with the substances composing the dyeing solution and the wax compounds. Ten subjects were given the following five patches: (1) the solution of soap used for dissolving orthotolueneazobetanaphthol (p_H, 10.9); (2) the emulsion of waxes used for coating the oranges, consisting of 10 per cent carnauba wax and 90 per cent paraffin emulsified in oleic acid, soap, shellac and water; (3) a 2 per cent solution of oil yellow AB, dissolved in liquid petrolatum; (4) a 2 per cent solution of oil yellow OB dissolved in liquid petrolatum, and (5) a 2 per cent solution of orthotolueneazobetanaphthol in liquid petrolatum.

The patches were removed from five subjects at the end of twenty-four hours, and there was only one reaction found, an erythema at the site of the first patch in one subject, who was probably sensitive to soap or alkali. At the end of seventy-two hours the patches were removed from the remaining five subjects, and no reactions were found under any of the patches. At the same time the five subjects from whom the patches had been removed at the end of twenty-four hours were examined for delayed reactions, and none were found.

Six other volunteers were tested with the three dyes previously mentioned, with a solution of sulfonated oil used for dissolving oil yellow OB and oil yellow AB and with the emulsion of mixed waxes described before. The patches were allowed to remain on for forty-eight hours, and on their removal there were no reactions. The results of these patch tests, combined with the fact that there was no dermatitis which could be attributed to the dyes or the waxes in any of the packing

plants inspected, showed that these dyes and waxes are not general cutaneous irritants. Hence, if any person should be irritated by them, the irritation would be due rather to his hypersensitivity than to the irritating properties of the dyes or the waxes.

The soap solution used for dissolving one of the dyes was shown to irritate one of the ten persons on whom it was applied as a patch test. This solution, however, is automatically washed off the orange peel after the fruit comes out of the dye bath and before it is waxed, so that it would be impossible for any one handling the oranges to be affected by it.

The dye on the "color added" orange is completely covered by a coating of wax and can come in contact with the skin of the handler of the orange only if the wax is rubbed off. In patch tests with the peel of a "color added" orange only the wax will touch the skin to which it is applied, unless the peel is cracked open so as to break the wax. In that case the irritating oils contained in the oil cells of the orange peel also will touch the skin. Thus, if a positive reaction is obtained, it cannot be definitely determined whether it is due to the irritating oils or to the hypersensitivity of the subject to either the dye or the wax. In order to determine whether the dye, the wax or the orange peel itself is the irritant, patch tests should be performed with each of these substances separately. In testing with citrus peel one must keep in mind the fact that citrus oils are general irritants and if allowed to touch the skin will cause reactions in normal persons. It must be kept in mind, too, that citrus fruit is "processed" in preparation for selling, and it is difficult to ascertain from the appearance of the fruit the various chemicals which may be deposited on the peel.

SUMMARY

The cutaneous hazards in the citrus fruit industry are:

In growing—dermatitis from fertilizers and insecticides and wounds from citrus thorns and splinters from boxes.

In packing—dermatitis from washing solutions and from hypersensitivity to citrus oils.

In canning—dermatitis and paronychia among peelers, reamers and sectioners, due to hypersensitivity to citrus oils and juices.

No cases of dermatitis were encountered which could be attributed to the dyes used to color the oranges.

CONCLUSIONS

1. Spreaders of fertilizer and handlers of insecticides should wear as protective clothing rubber gloves, aprons and goggles.

2. Pickers should wear leather gloves and wrist bands.

3. Packers should wear rubber gloves.

4. Peelers, reamers and sectioners should wear rubber gloves.

5. Packing and canning operations should be mechanized to as great an extent as possible.

6. While some oranges are treated with ethylene, washed with alkaline solutions, dyed and waxed in order to be more marketable, this treatment, if properly carried out, leaves nothing on the peel which constitutes a cutaneous hazard to the consumer. This is substantiated by the fact that, while millions of boxfuls of dyed oranges have been consumed since producers in Florida began to color oranges, only two cases of dermatitis have been reported that were attributed to hypersensitivity to orange dye. Nor are the waxes used on oranges (carnauba and paraffin) general cutaneous irritants.

7. It is possible that a few persons may be found whose skin is hypersensitive to the dyes used on oranges, but no more than are hypersensitive to the dyes used on other articles of food.

8. Whether the consumption as food, in the form of marmalade or in beverages, of citrus peel which has gone through the processes described constitutes a systemic hazard to the health of the public is not reported on, as this question is not within the scope of this paper.

STIGMATIZATION

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"Le coeur a ses raisons que la raison ne connait pas."—Blaise Pascal

In a recent publication [1] I reviewed data concerning the psychogenic aspects of somatic reactions expressed cutaneously and the various diseases of the skin believed to be psychogenic. Properly speaking, one cannot label a cutaneous disease psychogenic, since there are no features indicative of psychogenesis. The application of the term to diseases of the skin is based on a post hoc conclusion.

In a study of the psychogenesis of diseases of the skin the occurrence of various cutaneous reactions and, indeed, of cutaneous diseases following suggestion in hypnosis comes close to fulfilling the principle of inductive reasoning—"The same cause under the same circumstance produces the same effect."

Stigmas afford admirable material for the study of psychosomatic reactions, so far as the skin as an organ of expression is concerned. In the introduction to her volume on emotions and bodily changes,[2] Dunbar wrote:

> The problem of psychosomatic interrelationships is continually a stumbling block to the specialist in any phase of scientific research or personality study. Now and then a courageous investigator has taken it up, examined it, considered methods of studying it, only to relegate it to the philosopher again.

I believe this statement applies admirably to the study of the religious stigmas, the history of which is imbued with mysticism.[3]

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1. Klauder, J. V.: Psychogenic Aspects of Skin Diseases, J. Nerv. & Ment. Dis. **84**:249, 1936.

2. Dunbar, H. F.: Emotions and Bodily Changes, New York, Columbia University Press, 1935.

3. It is desirable to discuss the meaning of the word mysticism. Historically, in the Christian church it meant contemplation, but in modern use it has been applied to many things. The following definitions by different writers may serve to show its real meaning: "My mind in the flash of a trembling glance came to Absolute Being.—That which is" (St. Augustine: "Confessions"). "A direct and objective intellectual intuition of Transcendental Reality" (Sharpe, A. B.: Mysticism, St. Louis, B. Herder Book Company, 1910) "Mysticism is the Art of Union with Reality. The mystic is a person who has attained that union in greater or less degree; or who aims at and believes in such attainment" (Underhill, Evelyn: Mysticism, New York, E. P. Dutton & Co., Inc., 1930). "The soul's

A revival of study of the stigmas is pertinent, since there is a present day stigmatist, Thérèse Neumann, of Konnersreuth, Germany.[4] Examination of her stigmas motivated me to write this report. A study of the stigmas, moreover, appears to me to fit in with the present trend of psychologic study of disease, which impresses me as being tinged with mysticism. I refer to the concept of disease as a disturbance of the relationship between organism and environment, a study of man as a component part of his environment—the "man-environment unit"—the reaction of man to reality and to fantasy (Draper[5]). One step further in this concept of man as a part of the universe leads one into mysticism in the broadest sense—a relationship of the self to the not-self, of a part to the whole.

Stigma,[6] a Greek word, means a spot, a sign, a wound or a mark branded on a slave. In a figurative sense the word has been used to

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possible union in this life with Absolute Reality" (Rufus Jones). " . . . the art of finding our emotional relationship to the world conceived as a whole" (Ellis, Havelock: The Dance of Life, Boston, Houghton Mifflin Company, 1929).

One's concept of mysticism is related to one's ontological concept. Mysticism has a theistic, a pantheistic and indeed a nonreligious significance, if "nature ecstasy" is to be included in the term. The ecstasy in "nature ecstasy" may be nonreligious or vaguely religious in its content. The "cosmic consciousness" of Bucke may here be included (Bucke, R. M.: Cosmic Consciousness, New York, E. P. Dutton & Co., Inc., 1931). Mysticism may have a practical significance. In the sense of Evelyn Underhill, "The active man is a mystic when he knows his activities to be part of a greater activity."

Yogism, Buddhism, Sufism, Neo-Platonism and the doctrines of St. John of the Cross, Madame Guyon, Blake and Whitman are representative of different phases of what is called mysticism.

The craving to get out of oneself, the desire for infinite enlargement, escape and union is common to all mystic states. Indeed, the lure of the unknown shapes the mystic faculty of the human being. To include all phases, I would define mysticism as an enlargement of one's conscious mind and an experience of personal identity in the infinite universe.

4. C. Simon (Les stigmates cutanés des mystiques, Bull. méd., Paris **47**:667 [Oct. 21] 1933) and Benon (Note sur l'extase, ibid. **49**:267 [April 20] 1935) mentioned another living stigmatist, Marie-Julie Jahenny (born in 1850) at Blain near Nantes. No description of her stigmas was given, nor have I been able to find such a description elsewhere.

5. Draper, G.: The Common Denominator of Disease, Am. J. M. Sc. **190**:545, 1935.

6. A popular meaning of the word stigma, given in Webster's dictionary, is a mark made with a branding iron, a mark of infamy or disgrace. It is difficult to correlate this meaning with the one signifying the wounds of Christ. The following may serve as an explanation: At the time of the crucifixion of Christ it was decreed by Roman law that Roman citizens should be killed by the sword and others by crucifixion, a means of death accorded only to lower criminals. Hence the wounds of such a death were marks of infamy.

signify the counterparts of the five wounds in Christ's body appearing on persons affected in a particular way by the Passion.

According to Jacobi [7] there are three hundred recorded instances of stigmas.[8] Of this number, forty-one appeared in men. Of the men with stigmas perhaps the best known, and indeed the first of whom there is a record, was St. Francis of Assisi, in the thirteenth century.

Stigmatists have been of all ages and all stations in life. Many nationalities have been represented. There has been some variation in the character of the stigmas and in their size, number and location. The stigmas have been presented as scars, as localized pain, as wounds and as bleeding through the skin at regular intervals. Both surfaces of the hands, the feet, the right side of the chest and a circle around the head are typical areas involved. In some stigmatists not all these areas were involved, and in a few a stigma was on the left rather than the right side of the chest.[9]

Many of the stigmas have been fraudulently produced; others were accepted as genuine by medical writers. The nineteenth century produced about thirty stigmatists. Since St. Francis of Assisi, some well known stigmatists have been St. Catherine of Siena (1347-1380), Lucie of Narni (1476-1544), Catherine of Ricci (1522-1590), Veronica Guiliani (1660-1727), Anna Katherina Emmerich (1774-1824), Maria Moerl of Tyrol (1812-1883), Maria Domenica Lazzari (1815-1850), Juliana Weisskircher (1824), Maria Beatrix Schumann (1853), Louise Lateau (1850-1883) and Gemma Golgani (1878-1903).

In modern times the following four stigmatized persons have been studied by physicians from a scientific point of view: Louise Lateau by Warlomont,[10] Madeleine X at the Salpêtrière in Paris by Paul Janet,[11] Pio of Pietrelcina (1887) by Drs. Romanelli, Bignami and Festa [12] and Thérèse Neumann by Ewald,[13] professor of psychiatry at Erlangen.

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7. Jacobi, W.: Die Stigmatisierten, Beiträge zur Psychologie der Mystik, Munich, J. F. Bergmann, 1923.

8. In addition to Jacobi's volume, discussion of stigmatization is furnished by: Görres, J.: Die Christliche Mystik, Ratisbon, 1836-1842, vols. 1-4; La mystique chrétienne, (French translation, Paris, 1854); Imbert-Gourbeyre, A.: La stigmatisation, Paris, Vic & Amat, 1895, vols. 1-2.

9. Simon expressed the belief that the location of stigmas on the left side of the chest is conditioned by a face to face mental representation of Christ, in which the right side of Christ corresponds to the left side of the stigmatist.

10. Warlomont, E.: Louise Lateau. Rapport médical sur la stigmatisée de Bois-d'Haine, fait à l'Académie royale de médecine de Belgique, au nom d'une commission, Paris, J.-B. Baillière & fils, 1875.

11. Janet, P., cited by Simon, C.: Les stigmates cutanés des mystiques, Bull. méd., Paris **47**:667 (Oct. 21) 1933.

12. Festa, G.: Padre Pio da Pietrelcina, Rome, 1926.

13. Ewald, G.: Die Stigmatisierte von Konnersreuth, München. med. Wchnschr. **74**:1981 (Nov. 18) 1927.

Ewald wrote that the parents of Thérèse Neumann refused the suggestion of ecclesiastical personages that she be isolated in a hospital. Instead, Dr. Ewald and Dr. Seidl, the family physician, were assigned for a two week medical observation of Thérèse Neumann. Four nursing sisters were in constant attendance and were given detailed instructions for a strict surveillance of their charge.

The following history is abbreviated from Ewald's report:

In March 1918 a fire occurred in the barn of a neighbor of Thérèse Neumann's employer. When engaged in carrying buckets of water she suddenly felt a cramp-like pain in the back. From this time she felt pain when she attempted to lift a heavy object, lost appetite, had insomnia, walked around slowly and was unable to work. She was hospitalized for six weeks—the diagnosis was hysteria after shock. Menstruation disappeared for one year, after which it returned sparingly. It has been absent since 1920. She acquired the conviction that she was ill. After discharge from the hospital she was not entirely well and was able to do only light housework.

In the summer of 1918 she complained of shimmering light in the line of vision, and vision became impaired. In October 1918, when attempting to lift a heavy object, she overexerted herself and from then on was unable to walk. She became so ill that her parents thought she was going to die. Vision was much impaired. When an attempt was made to perform an ophthalmoscopic examination, she had what was regarded as a hysterical convulsion. Her physician, to appease her, told her that a vertebra was probably displaced. No roentgen examination was made. All subsequent examinations showed the spine to be normal. About January 1919 she applied for accident insurance and was given the usual accident rate.

She became bedridden, paralyzed, blind and for about one week completely deaf. Bed sores appeared at sites of pressure, on the inner aspects of the knees and the ankles, as a result of constant lying on her side with the legs held firmly together. The bed sores healed without scars. She vomited blood and bled from the ears.

According to Ewald, she presented a picture of hysteria. He commented on the bleeding from the ears and the stomach which continued despite the fact that she did not menstruate.

From 1920 to 1925 she had no medical attention but was nursed by her parents. According to Ewald, she was frequently visited by her parish priest, who, Ewald stated, may have pointed out to her the sufferings of Christ, so that Thérèse longed to emulate the sufferings of the martyrs and bore her sufferings with a glad heart.

During the time of her illness her father had rheumatism. Thérèse asked her pastor if she could pray to little St. Thérèse that she might suffer instead of her father. Soon thereafter she had rheumatic pain in the left arm, and it became flexed. It remained this way for three months. In 1922 a young seminarian had some pharyngeal affliction which threatened to interfere with his studies. Thérèse prayed to her patron saint, little St. Thérèse, that she might suffer in place of the seminarian. The following day she experienced difficulty in swallowing, which persisted. This caused her to take only fruit juices and milk. At the time of Ewald's report it was said that she took no food or drink.

According to Ewald, the time was appropriate for her cure, since she emulated the example of the saints. If the saints could cure others, then she, who took the sufferings of others on herself, could be cured. The saints could cure her. On

the day that little St. Thérèse was beatified, April 29, 1923, Thérèse Neumann was suddenly cured of her blindness. Two years later, May 17, 1925, she had a vision in which little St. Thérèse revealed to her the possibility of cure. She was found lying in bed with a radiant face and exclaimed that she saw a bright light. Her pastor was called. She sat up in bed and said that she had talked with St. Thérèse and that she could now walk. She got out of bed and with some support walked around the room.

Ewald remarked that from a psychologic point of view the thought that she wanted to get well and her faith that she would get well were what produced the cure. It was autosuggestion. This experience instilled in her mind the thought that she was the object of divine grace. Soon after this occurrence, she had what Dr. Seidl diagnosed as acute appendicitis, the symptoms of which were said to be typical. Arrangements were made for an operation, when rather suddenly the symptoms disappeared. Dr. Ewald commented on the possibility of hysteria or of an abscess penetrating into the rectum.

Physical Examination.—The physical examination gave essentially negative results. The corneal reflex was present and the laryngeal reflex absent. There was no disturbance in sensation or in the superficial and deep reflexes. There was no dermatographism.

The Stigmas.—The time of the first appearance of the stigmas on the dorsa of the hands is obscure. Apparently they appeared suddenly. Dr. Seidl did not see Thérèse until after their appearance. There was no prodromal pain. The patient denied knowledge of the stigmas of Louise Lateau and of Anna Katherina Emmerich. Soon after the appearance of the stigmas she began having trances and ecstasies, and at that time bloody tears first appeared; later new stigmas appeared over the heart and on the feet. On Nov. 6, 1926, during ecstasy, bleeding appeared at three places on the scalp. Now there are eight places. After 1927 stigmas appeared on the palms and the soles. In the beginning there was a constant but slow oozing of blood from the stigmas; later only some of them bled, and only on Friday. During the Passion of Holy Week there was bleeding from all the stigmas.

As recorded by Ewald, the stigmas were not penetrating wounds, although there was a subjective sensation of penetration. On the dorsa of the hands and the feet they were the size of a 10 pfennig piece and slightly raised and presented a dark crust, despite the absence of bleeding for three months prior to the time of the examination. The crusts did not become detached and fall off. Their surfaces were dry and glazed. When blood oozed through the crust the appearance was that of a fresh clot of blood; at other times the color was dark. Signs of inflammation were absent. The skin at the periphery of the crusts was thin and drawn in. The stigmas on the palms and the soles were about half the size of a lentil and three cornered and presented the same appearance as those on the dorsa of the hands. The stigma on the chest was over the fourth rib close to the sternum; the outline was oblique, and the crust was less elevated and dark brown. Seidl, who witnessed bleeding of the stigmas, described the appearance of an edematous elevation above the level of the skin, as though it had been separated from the upper epithelial layers of the skin. Through a magnifying glass fluid was seen to appear in a manner comparable to the formation of a drop of perspiration. It became bloody and rolled away. When examined microscopically it was seen actually to be blood.

I examined Thérèse Neumann's stigmas about nine years after Ewald's report. The one on the dorsum of the right hand was appar-

ntly a flat, dry, dark clot of blood. It was slightly elevated and almost perfectly square, with a diameter of about 1.5 cm. The surface was dry and shiny and apparently had not been adherent to the fish-net glove which had just been removed. The skin around the clot was normal in color and appearance, wrinkled and firmly adherent to the clot. There was no evidence of inflammation,[14] ulceration or destruction of tissue. Features which made the appearance distinctive and unlike that of an ordinary hemorrhagic crust were the square outline and the flat, glazed, ironed-out appearance. The clot did not rest on the skin but appeared to be part of it and was firmly adherent to the skin throughout its entire extent. Apparently it could not have been easily removed.

The stigma on the dorsum of the left hand presented the same features as the one on the right hand, except that it was larger, the diameter being about 1.75 cm. Across the forehead the stigmas were pinkish red, sharply outlined, pear-shaped, congestive areas about 0.5 cm. long. The skin was intact, and there were no crusts. Similar areas encircled the head. During the ecstasy, I was informed, they became vividly red; blood may exude, and the stigmas on the hands may bleed.

I tested the sensation of the skin of the arms with the dull and the sharp end of a pin. The response was normal. The corneal reflex was present. I was told that on one occasion during an ecstasy an insect had been observed to walk across the patient's cornea without producing a reaction.

Thérèse Neumann appeared to be in good health and of normal weight. She perspired freely in the sun. Although I interrupted her at work in the garden she was courteous. She impressed me as being emotionally normal, plain and humble. She did not exploit or talk about herself or the stigmas; on the contrary she was reticent and showed them reluctantly.

Bloody Tears.—As reported by Ewald, the conjunctiva was found to be normal before an ecstasy. There was no evidence of trauma. Dr. Seidl observed that the tears suddenly became bloody and clotted as they ran down the face. Examination showed the conjunctival sac to be filled with a fluid which on microscopic examination proved to be blood. It was thought that blood was not secreted directly from the lacrimal glands but that the tears were mixed with blood after being secreted.

The Ecstasy.—As recorded by Ewald, the ecstasy began every Thursday between 11 and 12 o'clock and lasted until Friday afternoon. Thérèse would awaken suddenly from sleep, partly sit up and remain motionless for a short period. She would be deadly pale, with eyelids half closed and hands stretched out; blood-tinged tears would run down her face and clot on her chin and neck. After five

14. In stigmas accepted as genuine by medical writers, the absence of inflammation and of pus have been emphasized. Warlomont,[10] Laignel-Lavastine, M., and Abadie, A.: Notes sur trois stigmatisés (Véronique Guiliani, Lucie de Narni et le Père Pie de Pietrelcina) étudiés objectivement par des contemporains, Bull. Soc. franç. d'hist. de la méd. **27**:106, 1933.

or ten minutes she would sink back into the pillows and appear exhausted. The foregoing sequence would be repeated at intervals of ten or fifteen minutes for the entire twelve or thirteen hours. The final ecstasy would last an hour. During that time the twenty layer gauze compress on the stigma over the heart would become saturated with serous bloody fluid. The headpiece would show a small spot of blood. The stigmas of the hands and feet would not bleed. When asked questions she would describe in a low voice what she had seen. Apparently she would live the whole scene at Calvary, following Christ at each step. In the final hour, when she would experience the crucifixion, she would sit for the whole hour in a half-upright position, with arms extended and eyes wide open and staring.

The expression of the face would change, expressing sorrow and pain. Finally she would fall back as though dead. In the afternoon there would usually be an outbreak of perspiration, after which she would remain partly asleep for the rest of the day. The following morning she would have completely recovered.

She has described her visions as not like pictures, but as vivid and colored. Her description of Jerusalem is said to be accurate. The Aramaic dialect is said likewise to fit properly the person whom she quotes.[15] During the fourteen day period of observation she slept one and one-half hours on three nights, a little over one hour on three and one hour on two. During the two weeks' observation her temperature was mostly normal; her pulse was regular but varied in frequency during ecstasies. No food was taken; 3 cc. of water was taken to swallow the Host. Urine was passed twice, 345 cc. and 180 cc., respectively. (The analysis is recorded in Ewald's report.) There was no bowel movement. She vomited twice, once blood and the other time mucus and blood. Laboratory examination showed no residue of food in the vomitus. Her weight was taken at the beginning and the end of the period of observation. There was a fluctuation of a few kilograms; the final weight, however, was 55 Kg., the same as at the beginning of the observation. Ewald commented on these curious features and concluded that it would be necessary to admit Thérèse to a hospital for further study.

Gerlich[16] exhaustively studied the case of Thérèse Neumann from observation and information derived from some weeks' residence at Konnersreuth. He challenged the diagnosis of hysteria and called attention to the lack of a roentgen examination after the first injury.

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15. Maere (Thérèse Neumann à Konnesreuth, Ann. et bull. Soc. roy. de méd. de Gand **10**:123, 1931) discussed this. The following paragraph is quoted from him: "On Nov. 4, 1927, during the period which follows the ecstasy, Professors Wutz and Gerlich asked her: 'Tell us, Thérèse, what are the words of Christ at the moment of his death?' Answer: 'Abba bejadach afked ruchi' (Father, into thy hands I commend my spirit). Question: 'And what has he said before that?' Answer: 'Schalem kalachi' (It is finished). Question: 'And what did he say when he was thirsty?' (Answer: 'Essche.') Question: 'What did he say to one of the malefactors?' Answer: 'Teje emmi Barbadetta' (Today thou shalt be with me in paradise).

"The professors said that these foreign words corresponded exactly to the pronunciation of the Aramaic." R. W. Hynek (Konnersreuth: A Medical and Psychological Study of the Case of Therese Neumann, New York, The Macmillan Company, 1932) quoted Bauer, professor of semitic philology at Halle, who stated "The fact that it is real Aramaic is absolutely incontestable."

16. Gerlich, F.: Die stigmatisierte Therese Neumann von Konnersreuth, Munich, Josef Kösel & F. Pustet, 1929.

He emphasized the three subsequent injuries sustained by Thérèse Neumann, which Ewald did not mention. He expressed the belief that injury to the spinal cord and the brain could explain her symptoms and that Thérèse had a subluxation of two lumbar vertebrae and an intracranial hemorrhage. He further pointed out that her ability to walk returned gradually between June and September 1925 and not suddenly, as one is led to believe from Ewald's report.

COMMENT

The theory of Thérèse Neumann's stigmas being self produced is untenable. There is no way of producing cutaneous lesions of the nature of stigma except by external agents. Oozing blood occurred from one or more of her stigmas each week. At the time I saw her the stigmas had been present for about eight years. To have been self produced they would have required external application or manipulation many hundreds of times. The appearance of the stigmas and the absence of inflammation, ulceration or destruction of tissue excluded this possibility

Ewald expressed the belief that Thérèse Neumann's stigmas are genuine and that deception has been excluded for the following reasons: 1. Microscopic examination showed that the stigmas exuded blood. 2. Several physicians noted that the onset of bleeding was spontaneous and the quantity of blood such that it could not have been produced by artificial means without the production of scars, especially since bleeding was frequently repeated. These considerations particularly applied to the bloody tears. 3. The stigmas on the chest exuded not pure blood but serous fluid tinged with blood, which could not have been produced artificially. 4. There was no evidence of pus formation, which could not have been avoided if artificial means had been used. 5. The change in the appearance of the stigmas during ecstasy suggested the operation of a spontaneous somatic change. 6. The supervision of Thérèse Neumann during the two weeks' observation was so thorough that it is most improbable that artificial means could have escaped notice. 7. The cessation of menstruation before the appearance of stigmas and the inclination of the skin to necrosis favored the appearance of bleeding from other places in the body.

Of other medical writers who have expressed the opinion that Thérèse Neumann's stigmas are genuine, mention may be made of Jacobi,[7] Clément Simon,[17] Birnbaum[18] and Maere,[19] who wrote:

17. Simon, C.: Les stigmates cutanés des mystiques, Bull. méd., Paris **47**:667 (Oct. 21) 1933.

18. Birnbaum, K.: Konnersreuth in ärztlicher Beleuchtung, Deutsche med. Wchnschr. **59**:302 (Feb. 24) 1933.

19. Maere: Thérèse Neumann à Konnersreuth, Ann. et bull. Soc. roy. de méd. de Gand **10**:123, 1931.

I for my part do not believe that Thérèse Neumann utilizes any deception; her attitude is natural, simple, without ostentation; she has perfect mental equilibrium, aside from her ecstasies she does not present any characteristic of hysteria or dream delirium; she has inexplicable phenomena, but, because they are inexplicable, do they not exist?

A few writers have explained stigmas as vicarious menstruation, as Majocchi's disease, as a blood dyscrasia, as a result of pressure of the finger-nails against the palms during the ecstasy and as Ehlers-Danlos syndrome. These explanations are not acceptable. Clinically Thérèse Neumann's stigmas are unlike any lesion that characterizes diseases of the skin. Genuine stigmas, I believe, should be classified among exotic dermatoses.

The spontaneous occurrence of cutaneous hemorrhages and ecchymoses in psychopathic subjects, although rare, has been reported by Schindler [20] and by Jacobi.[21]

Jacobi [7] wrote that among the Mohammedans there are said to be stigmatized persons whose stigmas appear while they are contemplating the battle wounds of their prophet. He cited the following recorded instances of phenomena resembling stigmas, appearing in circumstances unrelated to religious ecstasy:

Pabst's patient was the sister of a soldier who was condemned to "run the gauntlet." At the hour assigned for the punishment she felt, when at home with her family, the sensation of the wounds her brother was receiving. In an ecstasy-like state, moaning and groaning, she fainted and was placed in bed. It was discovered that she bled from woundlike lesions on her back.

There was the case of a man on whom, when he witnessed in great fear the violent combat of two men, woundlike cutaneous lesions appeared and later bled.

Another case was that of a woman, who in a vivid dream was given a rose. After awakening she felt a burning sensation on her arm, and at the place there appeared the outline of a rose, which remained for eight days.

Discussion of the pathogenesis of the stigmas from a medical point of view involved consideration of the following factors, which I have discussed elsewhere:[1] (1) the various cutaneous lesions produced by suggestion in hypnosis and following the sight of accident or suffering;[22] (2) the peculiar lability of the vasomotor apparatus in psycho-

20. Schindler, R.: Nervensystem und spontane Blutungen mit besonderer Berücksichtigung der hysterischen Ecchymosen und der Systematik der hämorrhagischen Diathesen, Berlin, S. Karger, 1927.

21. Jacobi, E.: Psychogene Spontanblutungen der Haut, Arch. f. Psychiat. **88**:631, 1929.

22. In the case of stigmas that have been accepted as genuine and which have disappeared, the role of suggestion in causing such disappearance should be considered. For example I. Matko (Die stigmatisierten Jugoslaviens, Wien. med. Wchnschr. **83**:613 [May 27] 1933), in writing of stigmatists of Jugoslavia, mentioned the case of Jerica, a peasant girl, whom he accepted as a genuine stigmatist. Her pastor urged her to pray for the disappearance of the external symptoms, after which bleeding ceased and the stigmas disappeared; the pain remained.

pathic persons manifested in disorders of the peripheral circulation;[23] the function of the skin as an important organ of expression, an "Erfolgsorgan" comparable only to the eye; (4) the possibility that asceticism and mental training of a religious or a nonreligious kind, which give impetus to contemplation, an integral part of all mystic states, arouse certain latent powers of which William James wrote or change the "thresholds of exceptional mobility," which, according to Evelyn Underhill,[24] all mystics have,[25] and (5) the somatic representation of psychic events. Feeling can penetrate deeper than thought. In this regard the tremendous nature of the stimulus and the intense mental make-up of stigmatists should be recalled. Maréchal[26] said:

> No artist's vision was ever of a more concentrated richness, more terrific in its power of evocation, or more violently tense in its dynamism, than this simple and fixed gaze of the contemplative on God.

1934 Spruce Street.

23. H. Haxthausen (The Pathogenesis of Hysterical Skin-Affections, Brit. J. Dermat. **48**:563, 1936) employed a variety of cutaneous tests and failed to note any difference in reactivity between the skin of hysterical and of normal persons.

24. Underhill, E.: Mysticism, New York, E. P. Dutton & Co., Inc., 1930.

25. She stated: "A very slight effort, a slight departure from normal conditions will permit their latent or subliminal powers to emerge and occupy the mental field."

26. Maréchal, J.: Studies in the Psychology of the Mystics, translated by Algar, London, Burns, Oates & Washbourne, Ltd., 1927.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

ACUTE LUPUS ERYTHEMATOSUS DISSEMINATUS. BERNARD S. DENZER and SIDNEY BLUMENTHAL, Am. J. Dis. Child. **53**:525 (Feb.) 1937.

This is the report of a case of fatal acute disseminated lupus erythematosus in a 7 year old girl. During an afebrile period an abscessed tooth was extracted. This resulted in an elevation of the temperature to 102 F., and the general condition became decidedly worse. The urine showed albumin, casts and red blood cells. There were 10,000 white blood cells at the time of admission, but the count later diminished to 4,900. The autopsy revealed, among other things, mural endocarditis of the right ventricle and focal necrosis of the liver. The renal lesions were chiefly confined to the glomeruli and consisted of a homogeneous thickening of the capillary walls. The authors include a critical survey of the literature on the concept of lupus erythematosus disseminatus as a systemic disease.

NELSON PAUL ANDERSON, Los Angeles.

STUDY OF THE OSSEOUS REMAINS OF A PRIMITIVE RACE WHO ONCE INHABITED THE SHELTERS OF THE BLUFFS OF THE OZARK MOUNTAINS. ELMER G. WAKEFIELD, SAMUEL C. DELLINGER and JOHN D. CAMP, Am. J. M. Sc. **193**:223 (Feb.) 1937.

Remains of more than 200 prehistoric bluff dwellers in the Ozark Mountains were examined for pathologic changes. Several tibias showed evidence of osteitis resembling that caused by syphilis, but there was not sufficient evidence of syphilis in the rest of the skeletons in which these tibial changes were found to warrant such a diagnosis. These changes in the tibias could have been the results of trauma.

THE EFFECT OF TRYPARSAMIDE ON THE OPTIC NERVE. WILLIAM L. BENEDICT and H. P. WAGENER, Am. J. M. Sc. **193**:286 (Feb.) 1937.

Benedict and Wagener review the pertinent literature in an attempt to answer three questions: (1) Does tryparsamide have a direct toxic action on the optic nerve? (2) Is atrophy of the optic nerve essentially a result of the primary disease of the central nervous system, and, if so, does the tryparsamide activate this disease in or cause its extension into the optic nerve? (3) Is the presence of atrophy of the optic nerve a contraindication to the use of tryparsamide?

They conclude that the incautious use of tryparsamide may result in serious damage to the optic nerves. Whether this damage is due to a toxic action of the drug or to an exacerbation of syphilis of the nerve is relatively unimportant. Tryparsamide may produce visual disturbance in cases in which the eyes were previously normal; under certain conditions it can be used even in cases of atrophy of the optic nerve. Examinations with the ophthalmoscope and the perimeter should be made for all patients who complain of disturbances of vision during the course of treatment with tryparsamide. The authors express the belief that prompt discontinuance of the drug at the first sign of organic involvement of the optic nerve will usually prevent permanent loss of vision.

LYNCH, St. Paul.

FURTHER STUDIES IN EXPERIMENTAL SYPHILIS. F. JAHNEL, Am. J. Syph., Gonor. & Ven. Dis. **21**:18 (Jan.) 1937.

Studies of experimental syphilis have usually been limited hitherto to a few laboratory species. Jahnel has shown in his work that many wild animals are

susceptible to syphilis and has made many successful and unsuccessful attempts to transfer syphilis to various animals. Attempts have been made in vain to transmit syphilis to dogs, pigs and frogs. The author has found the rellmouse (Siebenschläfer) to be of great interest in the experimental study of syphilis. During the seven months of the year in which that animal hibernates there is a decreased metabolism and a markedly lowered body temperature, which may go to 4 or 5 C., depending on the surrounding air. Syphilitic infection seems to disappear during hibernation in the rellmouse. Similar experiments with the dormouse have given identical results. Other authors have observed the cure of trypanosomal infection in other animals during a period of hibernation. The author discusses the factors that might be involved in the cure of syphilis in experimental animals during hibernation.

THE EFFECT OF ALCOHOL ON PENETRATION OF BISMUTH INTO THE CENTRAL NERVOUS SYSTEM. H. W. NEWMAN and A. P. RICHARDSON, Am. J. Syph., Gonor. & Ven. Dis. **21**:77 (Jan.) 1937.

It has been recognized for a long time that certain agents are capable of changing the permeability of the hemato-encephalic barrier to various drugs. Significant quantities of bismuth have been consistently found in the brain and the spinal cord of dogs after intramuscular injection of iodobismitol, in confirmation of cerebral penetration reported clinically and experimentally by others. The continued ingestion of large doses of alcohol markedly increases the penetration of bismuth into the central nervous system under these conditions. The significance of these results is discussed.

MAPHARSEN IN ANTISYPHILITIC THERAPY. G. D. ASTRACHAN, Am. J. Syph., Gonor. & Ven. Dis. **21**:81 (Jan.) 1937.

The author reports the results of treatment with mapharsen in 158 cases. He believes the preparation is a good antisyphilitic remedy and less toxic than neoarsphenamine. His results were better when mapharsen was used in conjunction with a bismuth preparation, especially when the two were given concurrently, than when mapharsen was used alone. Mapharsen is useful in latent and in late congenital syphilis. In spite of the fact that mapharsen seems to influence favorably the clinical manifestations and serologic reactions in early syphilis, the author believes that early syphilis should be treated with a more potent drug, such as arsphenamine or neoarsphenamine.

CONGENITAL SYPHILIS OF THE EYE. V. E. LENNARSON and P. C. JEANS, Am. J. Syph., Gonor. & Ven. Dis. **21**:90 (Jan.) 1937.

Lennarson and Jeans reviewed the records of a group of 247 congenitally syphilitic infants and children. "Of the entire group, 38 per cent were found to have eye lesions attributable to syphilis. The incidence of keratitis among all of the children over two years of age was 43 per cent with a maximum frequency of 57 per cent at eight years. Chorioretinitis was found in only one infant. It was present in 6 per cent of the entire group of older children and in 13 per cent of those whose fundi were examined. Optic atrophy was present in one infant. It was found in 4 per cent of the entire group of older children and in nearly 6 per cent of those whose fundi were examined. Among the children two years of age and over the Wassermann reaction of the cerebrospinal fluid was positive in an equal proportion of those with and those without syphilis of the eye. Among the patients with keratitis, the cerebrospinal fluid was positive with definitely less frequency than among the group as a whole."

REUTER, Milwaukee.

RECKLINGHAUSEN'S NEUROFIBROMATOSIS: CLINICAL MANIFESTATIONS IN THIRTY-ONE CASES. JOHN C. SHARPE and RICHARD H. YOUNG, Arch. Int. Med. **59**:299 (Feb.) 1937.

Sharpe and Young review thirty-one cases of neurofibromatosis observed in three years. Of the thirty-one patients, eleven were males and twenty females; they varied in age from 3 to 66 years. Seventy-four per cent had a family history of the disease.

Seven children showed only pigmentary changes, while the remaining twenty-four had both pigmentation and tumors. Osseous changes were present in seven and elephantiasis in two. The disease was complicated by deafness in five and mental disorder in one. A malignant transformation was observed in one patient.

In the majority of patients, pigmentation began in infancy and increased during puberty and pregnancy, most commonly in association with the appearance of tumors. In most cases the osseous changes began during infancy.

No causal relation to endocrinopathy was observed, but menstrual irregularity was frequent, and 72 per cent of the fifty pregnancies that occurred caused either the onset or an exacerbation of the disease. Sharpe and Young noted with interest that in one third of the pregnancies associated with exacerbation signs of the disease have developed in the offspring, while after pregnancies which did not cause the onset or an exacerbation neurofibromatosis has not been observed in the child.

The authors were impressed by the dynamic rather than the static concept of the pathologic changes, influenced by heredity, birth, infancy, childhood, adolescence and pregnancy. They concluded that avoidance of pregnancy offers the best opportunity for arrest of the course and control of the disease.

IMMUNIZATION OF RABBITS TO INFECTIOUS PAPILLOMATOSIS. RICHARD E. SHOPE, J. Exper. Med. **65**:219 (Feb.) 1937.

Multiple intraperitoneal injections of suspensions of either infectious or noninfectious glycerinated papillomas of rabbits immunized domestic rabbits and cottontails to papillomatosis. When given intraperitoneally, the noninfectious material, like that which was fully infectious, was capable not only of increasing the resistance of rabbits to papillomatosis but of eliciting the formation of specific virus-neutralizing antibodies.

The capacity of the noninfectious suspensions to immunize is considered as evidence that they contain the virus of papilloma even though none can be demonstrated by the usual infection test.

LYNCH, St. Paul.

THE HAEMATOPHAGOUS FLY MUSCA SORBENS, WIED., IN RELATION TO THE TRANSMISSION OF LEPROSY. W. A. LAMBORN, J. Trop. Med. **40**:37 (Feb. 15) 1937.

Agreement is almost general that the leprosy bacillus gains entrance to the tissues through the skin or the mucous membrane. The author discussed evidence showing that the theory of direct contagion does not seem to apply in a high percentage of cases. It was shown that a tropical African fly, Musca sorbens, deposited leprosy bacilli on foods after leprous material had been fed to it. Evidence indicated that the vitality of the bacilli was not impaired by passage through the fly. The author agreed with the views of Castellani and Chalmers that many facts favor the theory that leprosy is spread by insects.

LUPIFORM CUTANEOUS LEISHMANIASIS OF THE FACE. H. GOUGEROT and J. DELORT, Bull. Soc. franç. de dermat. et syph. **44**:59 (Jan.) 1937.

Gougerot and Delort observed lupiform leishmaniasis in a patient 18 years of age. In March 1936 a reddish orange plaque measuring 12 by 17 mm. and 5 mm. high appeared on the right side of the patient's nose. The surface of the lesion

was slightly scaly; the border was serpiginous, and there was no ulceration. Although the color was suggestive of lupus vulgaris, the course was much too rapid for that condition. The authors expressed the belief that a syphilid would have been more indurated and a leproma more transparent. The patient had been residing in Algeria, which made a diagnosis of leishmaniasis probable. Serum obtained by scarifying the lesion was stained with the May-Grünwald-Giemsa method, and numerous intracellular and extracellular Leishman bodies were demonstrated. Treatment with antimony salts caused no regression. Roentgen therapy was begun, and when the patient was last seen improvement was taking place.

Inguinal and Iliac Tuberculosis Adenitis Simulating the Disease of Nicolas-Favre. P. Lefèvere, Cochez and Fichet, Bull. Soc. franç. de dermat. et syph. **44**:253 (Feb.) 1937.

The observers reported a case of subacute inguinal and iliac adenitis in a man aged 56. The course of the disease was subacute, with remissions and exacerbations, and the clinical features were cellulitis, fistulas and elephantiasis. The Frei test was strongly positive, and there was enough response to therapy with antimony to seem to justify a diagnosis of lymphogranuloma venereum.

Some time later a cold abscess developed in the nuchal region, and pus from it caused tuberculosis in a monkey. Inoculations of pus from the abscess in the iliac fossa gave positive indications of tuberculosis. The diagnosis of tuberculous adenitis simulating lymphogranuloma venereum was then decided on.

Papular Petaloid Erythema. A. Civatte, A. Tzanck and C. Grupper, Bull. Soc. franç. de dermat. et syph. **44**:334 (Feb.) 1937.

On the basis of the observation of four patients the authors described what they believed to be a dermatosis which should be individualized under the name "papular petaloid erythema."

The eruptions appeared in healthy persons, and nearly always the initial lesion was situated on some articular fold, such as those in the popliteal or the inguinal region. The lesions then spread downward and upward to involve the trunk and the extremities. They were most numerous on the flanks, the abdomen and the front and sides of the thorax, stopping at the posterior axillary line. The back, the face, the hands and the feet were uninvolved.

The essential lesion was a small raised, sharply marginated papule varying in size from that of a pinhead to that of a lentil. The color was bright rose or red. The evolution of the papules was difficult to define, since the patients were observed but a short time. It seemed, however, that the lesions became gradually flatter and after slight desquamation disappeared.

The striking feature was the arrangement of the papules in round or circinate medallions resembling petals. Pruritus was present in all cases. The lesions evolved in cycles and were not accompanied with constitutional symptoms.

Histologic examination showed intracellular edema in the epidermis and mild spongiosis and an inflammatory infiltrate of mononuclear cells in the cutis.

The etiologic factors could not be determined. Syphilis, tuberculosis and dermatomycosis were ruled out. The authors believed that papular petaloid erythema was related to yet distinct from erythema multiforme.

Lichen Planus and Stovarsol [Acetarsone]. G. Hufschmitt, Bull. Soc. franç. de dermat. et syph. **44**:360 (Feb.) 1937.

The author concluded after using acetarsone by mouth in treating lichen planus that fairly constant good results are obtained in cutaneous lesions but not in mucosal lesions; that occasional aggravation of the disease occurs, and that acetarsone does not protect against recurrences. In cases in which the condition was resistant to acetarsone some success was obtained with irradiated ergosterol.

The author stated that lichen planus is rare in Alsace, France.

Laymon, Minneapolis.

EXPERIMENTAL STUDIES ON COPROPORPHYRINURIA DURING ARSPHENAMINE THERAPY. F. SCOLARI, Gior. ital. di dermat. e sif. **78**:5 (Feb.) 1937.

Scolari studied the rate of elimination of porphyrin in twelve patients with syphilis before and during therapy with arsphenamine. Eight of these patients showed a marked increase in the elimination of porphyrin in the urine during treatment with arsphenamine.

PECULIAR FORM OF PSORIASIS PUSTULOSA. L. PERUCCIO, Gior. ital. di dermat. e sif. **78**:65 (Feb.) 1937.

Peruccio reports the case of a generalized vesicopustular eruption in association with psoriasis, after the use of a weak salicylic acid ointment. He expresses the belief that the condition was the result of idiosyncrasy to salicylic acid and not true psoriasis pustulosa. Although the vesicopustular lesions developed into typical psoriatic lesions, Peruccio attributes this transformation to the Köbner phenomenon.

HISTOPATHOLOGY AND ETIOLOGY OF GRANULOMA ANNULARE. A. GRASSI, Gior. ital. di dermat. e sif. **78**:89 (Feb.) 1937.

Grassi reports two cases of granuloma annulare of the hands in patients with chronic pulmonary tuberculosis. Histologically the most characteristic lesions were large necrobiotic areas in the corium, surrounded by a thick infiltration of lymphoid and epithelioid cells, which usually developed around the blood vessels. Acid-fast bacilli were not found in the tissues, but inoculation of a fragment of the affected skin into a guinea-pig produced typical tuberculosis, associated with numerous acid-fast bacilli in the regional lymph glands. Grassi concludes that granuloma annulare should be considered classic tuberculosis rather than tuberculid.

PARDO-CASTELLO, Habana.

HISTOLOGY OF HUMAN SKIN: II. ON DIFFERENCES IN THE ELASTIC FIBERS OF THE SKIN ACCORDING TO SEX AND AGE. ISABURO EJIRI, Jap. J. Dermat. & Urol. **40**:216 (Dec.) 1936.

Studies were made of the elastic tissue of the skin of fifty subjects varying in age from less than 1 year to 77 years. The author arrived at the following conclusions:

Clusters may be found under the epidermis in persons above the age of 6 years, particularly in the face. Thus, there is no relation between cluster formation and age. Coarse granules appear in the third decade and are distinct in the fourth decade. Fine granules appear at the end of the fourth decade and are distinct in the fifth decade and marked in the seventh. Vitreous changes appear after the age of 40. Change in the elastic fibers in the middle part of the corium starts in the fourth decade and becomes distinct at its end. Changes in the lower part of the corium begin mostly at the end of the sixth decade and are distinct in subjects above the age of 60.

Changes in the elastic tissue begin at different ages according to the region. The intensity of the change increases with age. Changes are less intense in women than in men.

STUDIES ON CEREBROSPINAL FLUID IN SYPHILIS WITH MANIFEST SYMPTOMS, PARTICULARLY ON THE FRACTIONAL DETERMINATION OF PROTEINS. T. UEDA, Jap. J. Dermat. & Urol. **40**:219 (Dec.) 1936.

The author found pathologic changes in the cerebrospinal fluid in 19 per cent of 26 cases of early syphilis, in 43 per cent of 62 cases of secondary syphilis and in 32 per cent of 19 cases of tertiary syphilis.

In the first stage the cell count is always under 10, and the globulin reaction, the total protein and the colloidal gold reaction hardly transgress the normal

limits. In the second stage all reactions are more distinct; particularly, the cell count may be high. In none of the cases in the author's series was there a positive Wassermann reaction of the cerebrospinal fluid in the first, the second or the early latent stage.

The author never observed a case of syphilis with manifest clinical symptoms or of latent syphilis with a positive Wassermann reaction which was unaccompanied with any other positive reaction. Whenever the Wassermann reaction of the cerebrospinal fluid was positive, the other reactions were positive.

In the seronegative (first) stage pathologic changes in the fluid were present in 1 of 8 cases.

The author's observations are in accord with those of Ravaut, Königstein and Goldberger and of Wile and Stokes in regard to the proportion of positive reactions of the cerebrospinal fluid of patients with papular eruptions to those of patients with roseola, namely, 43 to 30. In cases of alopecia syphilitica the percentage of positive reactions was somewhat higher than that usually observed in the second stage.

In most cases the pathologic changes of the fluid responded to antisyphilitic therapy. The cell count became normal first. In some of the patients treated with small amounts of antisyphilitic remedies the therapy seemed to be provocative.

For the fractional determination of the protein content the author used the diaphanometric method, although he does not consider it perfectly satisfactory. He found the average amounts of total protein, of albumin, of globulin and of globulin precipitate higher in fluid removed during the first stage than in the control fluid. Although both protein fractions, albumin and globulin are increased, they are not changed in proportion. The average amounts of total protein and the protein quotient are higher in the second stage than in the first, and the amount of globulin is particularly increased.

EXPERIMENTAL STUDIES ON THE DISTRIBUTION OF A GOLD SALT IN THE ORGANISM: II. INFLUENCE OF A GOLD SALT ON THE RETICULO-ENDOTHELIAL SYSTEM. J. SANO, Jap. J. Dermat. & Urol. **40**:227 (Dec.) 1936.

In rabbits which had received 0.25 cc. of sodium aurothiophenolmetacarbonate intravenously, the congo red index was lowered during a short period, after which it rose to normal. This indicates possibly a functional stimulation of the reticulo-endothelial system. In animals which had received 3 cc. of the gold salt, the index, on the contrary, was considerably elevated; at the same time the animals were severely poisoned. This is to be explained by the involvement of the parenchymatous organs, particularly of the liver.

The author has observed that the congo red index stayed almost normal if the cells of the reticulo-endothelial system of a rabbit were blocked by india ink or if its spleen was removed. On the contrary it was markedly elevated when animals were previously given an injection of 0.5 cc. of 0.25 per cent phosphorated oil. This injection produced rapid disturbance of the parenchymatous cells of the liver, without any involvement of the Kupffer cells.

Seventeen rabbits were given intravenous injections of different amounts of the gold salt and examined after different intervals. Gold particles were found in the histiocytes by histochemical methods based on the reduction of gold salts by tin chloride. The gold particles are at first fine and gradually become coarser and often confluent. The number of free macrophages containing metallic granules corresponds to the size of the dose of the gold preparation administered and the length of the interval between the injection and the examination. At the same time, sections stained with the usual methods revealed intense congestion, sometimes hemorrhage, an increase in the number of macrophages and changes in the parenchymatous tissue except in the follicles of the spleen.

HISTOLOGIC STUDIES OF HUMAN SKIN: III. CHANGES ACCORDING TO REGION AND TO AGE, OF DIFFERENT ELEMENTS OF THE SKIN, WITH PARTICULAR CONSIDERATION OF CHANGES OF THE ELASTIC FIBERS WITH AGE. I. EJIRI, Jap. J. Dermat. & Urol. **41**:8 (Jan.) 1937.

The author has performed 718 biopsies of skin from 50 cadavers and studied the different layers and elements of the skin. The essential observations were as follows:

The granular layer was composed, according to the region, of from one to three and from two to four rows of cells, and no senile atrophy of this layer was noted. Slight formation of vacuoles around the nuclei was seen not only in old but in young persons. The number of rows of cells in the prickle cell layer varied, according to the region, from one to seven; as age increased there was diminution in the thickness of the prickle cell layer of the scalp and the face and hypertrophy developed on the extensor surfaces of the arms, the hands and the feet.

There were regional differences in epidermal peg formation. In some areas the pegs and papillae were elongated; in other areas they were absent, and the border between the epidermis and the cutis was a straight line. The hair follicles were dilated in some places. This dilatation was distinct and more marked in persons older than 50. The blood capillaries began to appear distinctly dilated in subjects above the age of 40, and this manifestation was particularly marked in subjects above the age of 50. Infiltration of cells into the cutis was limited to the vicinity of the vessels and sebaceous glands and consisted of connective tissue and round cells.

Degeneration of the collagen fibers took place in the papillary layer. There remained always underneath the epidermis around the hair follicles a narrow strip of connective tissue of so-called stratum subepitheliale cutis of Unna. The degeneration of collagen fibers varied according to the region, in some areas being marked and in others slight. It began at different ages, according to the region. There was a close relation between changes of the elastic tissue and those of the collagen fibers. Basophilic collagen, however, did not show any differences according to region or age or any relation to the changes in the elastic tissue.

DERMATOSCOPIC INVESTIGATIONS OF THE CAPILLARY LOOP IN LEPROUS SKIN. S. KOMATSU, Jap. J. Dermat. & Urol. **41**:13 (Jan.) 1937.

The author investigated dermatoscopically the blood vessels of the skin of 45 leprous patients, using as controls 110 normal subjects. He found most of the cutaneous blood vessels in the areas of hypesthesia to be dilated and winding. These changes were more marked in the macular and tuberous areas, but the number of vessels in those areas was not increased.

The apparently normal skin of leprous patients reacts to different irritants, such as heat, cold, mechanical irritation and intracutaneous injection of a 1:1,000 solution of epinephrine hydrochloride, as does the skin of healthy persons. The reactions of the affected skin vary; they may be positive or negative. The negative reaction is to be considered a result of degeneration of the nerve in this area. The degree of vascular reaction to the intracutaneous injection of 0.1 cc. of a 0.1 per cent solution of histamine depends on the degree of hyperemia of the injected area, independent of the other pathologic changes.

BLOOM, New York.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

LOUIS CHARGIN, M.D., *Chairman*

Oct. 5, 1937

HARRY C. SAUNDERS, M.D., *Secretary*

Sarcoid (Boeck); Osteitis Cystica Tuberculosa (Jüngling). Presented by DR. GEORGE M. LEWIS.

J. C., a man aged 25, presents an eruption on the face which developed seven years ago. It has since slowly progressed in extent, and changes in the bones of the hand have been noted. The patient is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

Examination reveals a triangular slightly elevated dusky red scaly patch, 3.75 by 1.5 cm., over the right zygoma. Lesions of varying size but of the same appearance are present on the left cheek and across the bridge of the nose. Lymph nodes in the posterior cervical regions are enlarged. All the fingers show enlargement of the distal phalanges. The little finger of the right hand and the ring finger of the left hand are shortened and distorted, and the skin shows inflammatory changes. A number of common warts are scattered over the palms and the backs of the hands.

A histologic examination of tissue from a lesion on the face was carried out elsewhere and revealed the structure of sarcoid. The roentgenograms showed cysts in the bones of the fingers. No focus of tuberculosis has been found. The tuberculin tests gave the following result: with a dilution of 1:1,000,000, negative; of 1:100,000, indefinite, and of 1:10,000, 1 plus.

DISCUSSION

DR. FRED WISE: This patient lives in Philadelphia and visits the clinic at irregular intervals. A series of intradermal tuberculin tests has given negative results—a fact pointing toward the anergic reaction peculiar to sarcoid of Boeck. The facial eruption resembles lupus erythematosus, but several injections of sodium gold thiosulfate have not caused improvement, according to the patient's statement. The lesions of the phalanges are in all probability an expression of Jüngling's cystic tuberculosis of the bones, a not infrequent accompaniment of sarcoid. The roentgenogram of the chest was said to have shown no abnormality.

DR. GEORGE M. LEWIS: The patient has been receiving gold therapy for the past six or eight weeks. The condition of the hands seems to be stationary.

A Case for Diagnosis (Generalized Seborrheic Eczema? Allergic Dermatitis?). Presented by DR. JOSEPH J. ELLER.

A. R., a man aged 41, is presented from the New York City Hospital. Fifteen years ago he had erysipelas of the face. Three and one-half years ago he was treated for a scaling erythema on the eyelids, the chin and the pubic region. This recurred in 1936 and spread to the scalp, the neck, the trunk, the genital region and the extremities. The condition improved for a short time with bland local applications, roentgen therapy and staphylococcus vaccine. The physical examina-

tion showed no abnormality except for the condition of the skin. The patient was admitted to the New York City Hospital in the early part of 1937 with generalized exfoliating erythema. There were numerous secondary pustules and fissures and moderate pruritus.

Examination of the urine showed no abnormality; the icteric index was normal, and the Wassermann reaction was negative. The blood count showed 47 per cent hemoglobin, 3,150,000 red blood cells, 10,400 white blood cells and a differential count of 41 per cent polymorphonuclear leukocytes, 40 per cent lymphocytes and 11 per cent eosinophils. The histologic examination of a section removed from the right arm showed a chronic pustular inflammation. The squamous epithelium seemed somewhat acanthotic and the rete cones slightly larger than normal. There were a few areas of mild spongiosis and a few polynuclear cells sprinkled in the epithelium. Occasionally there was a tiny focal accumulation of polynuclear cells in the more superficial parts. There was an occasional area of dyskeratosis. The rete pegs were sprinkled with polynuclear cells, lymphocytes, monocytes and fairly numerous eosinophils. The reticular portion of the corium was irregularly sprinkled with similar cells, except that the polynuclear cells were distinctly less numerous. Frequently these cells were seen in small focal collections around small vessels. Also present in these regions were numerous intracellular collections of granules of golden brown pigment. The basal layer of epithelial cells contained practically no pigment. The subcutaneous tissue and the deeper structures were normal. There were no vascular changes. A histologic diagnosis of chronic and subacute dermatitis was made.

The patient has had remissions and exacerbations with bland local applications and administration of liver extract, calcium, vitamins and autohemotherapy.

DISCUSSION

DR. OSCAR L. LEVIN: I believe that the term allergic dermatitis is being applied to too many conditions. This diagnosis is frequently too hastily made when another type of eruption may be present. The skin of this patient shows almost universal erythroderma, but in some places, as on the hands, it is possible to observe shiny and scaly patches of psoriasis. There are small spots on the palmar aspects of the hands and the fingers. The finger nails showed changes which are seen in psoriasis. I believe that the patient is suffering from generalized dermatitis secondary to psoriasis.

DR. LOUIS TULIPAN: I have an idea that many such chronic dermatoses are kept up by secondary low grade infections, and frequently it is possible to control a good part of the eruption by the application of one of the dye antiseptics such as methylosaniline (gentian violet) or brilliant green. I do not think the underlying condition can be cleared up with the dye antiseptics. In most cases eczema is aggravated or kept up by secondary infections.

DR. DAVID SATENSTEIN: I recall some patients at the New York City Hospital who came back four or five times. They would come in one time with generalized psoriasis; the condition would clear up, and they would go home and stay away for a few months and then return with dermatitis exfoliativa. They would then go home again and come back later with psoriasis. In this case I cannot understand where the question of infection enters. This eruption is a reaction of the skin to some unknown agent and has nothing to do with any known infection. As to therapy, I am much against making a pastel color chart out of patients with green dyes and blue dyes and so on, because when the next dermatologist comes along to examine the patient he cannot see anything. I believe in these cases the condition goes in cycles. I recall that the arsenical therapy was not indicated in this stage. I think the patient should be kept quiet and well fed, and on the skin only something to keep it from cracking should be used.

DR. DAVID BLOOM: This condition looks to me like generalized erythroderma. Psoriasis and leukemia have to be excluded by biopsy and a blood count. In most cases of this type no etiologic factor can be found. In some of these cases

fever therapy is of benefit. In one of my cases abscesses of the skin developed and fever lasted for several weeks. These factors probably contributed to the patient's complete recovery.

DR. A. W. GRACE: Apropos of what Dr. Bloom said, I wonder what danger there might be in treating patients of this sort with fever therapy. From the appearance of the skin, I imagine that the sweat glands are involved in the process. If that is so, there may be some danger in fever therapy. It would be interesting to know whether in cases in which fever therapy was employed the temperature was elevated only slightly or whether it rose as high as in the fever treatment of syphilis.

DR. FRANK C. COMBES: Several of the discussers have remarked on fever therapy. I think the discussion should be more specific as to type of fever therapy. I believe Dr. Bloom had reference to the use of foreign proteins for elevating the temperature.

DR. DAVID BLOOM: At the Bellevue Hospital intravenous injections of typhoid vaccine are used, the dose beginning at 0.1 cc. and gradually increasing to 1 cc. Patients frequently have a high temperature, from 104 to 105 F. In contradistinction to the severe headaches and chills associated with subcutaneous administration of typhoid vaccine as a prophylactic against typhoid infection, this intravenous administration of small doses is tolerated well and accompanied with mild constitutional symptoms. No ill effects from this treatment have been observed.

DR. OSCAR L. LEVIN: For several years I employed the artificial production of fever in the treatment of various dermatoses, with temporary good results, especially in erythroderma. Dr. Rosen has reported good results in various conditions of the skin. As for the production of fever by means of typhoid vaccine administered intravenously, I must say that the reaction is often severe, and I state from my own experience that, although changes may be produced in the condition and the patient be benefited, the administration of this form of treatment frequently has severe results and is not warranted.

DR. HOWARD FOX: While it is not pertinent to the discussion of this case, I must answer Dr. Levin by saying that at the Bellevue Hospital intravenous injection of typhoid vaccine has been employed in innumerable cases as a method of fever therapy. In no case have any ill effects been observed, and the injections have been uniformly well tolerated.

DR. JOSEPH J. ELLER: Dr. Levin may be correct that this patient may at some time or other have had psoriasis and that this chronic eczema that flares up is on the basis of an old psoriasis. However, in the past few months at no time have I seen any lesion typical of psoriasis in this patient.

A Case for Diagnosis (Pemphigus? Dermatitis Herpetiformis?). Presented by DR. JOSEPH J. ELLER.

R. F., a man aged 67, has an eruption which first developed behind the ears three years ago. This spread to the face and the back and later involved the entire body. There has been no remission of any consequence, and pruritus is marked. The patient was transferred from the Bellevue Hospital to the New York City Hospital in June 1937. At that time he presented generalized erythema on which were many bullae (flaccid and ruptured) and crusted lesions. These lesions varied in size from that of a pea to that of a coin and showed evidence of much scratching. There has been no involvement of the mucous membranes or orifices of the body. General physical examination shows no abnormality with the exception of the condition of the skin.

The Wassermann test and culture of the blood gave normal results. Chemical examination of the blood showed 120 mg. of sugar and 32 mg. of nonprotein nitrogen per hundred cubic centimeters. The Pels-Macht test showed 65 per cent toxicity. The blood count showed 72 per cent hemoglobin, 3,950,000 red blood cells and 12,600 white blood cells, with a differential count of 66 per cent poly-

morphonuclear leukocytes, 29 per cent lymphocytes, 1 per cent eosinophils, 2 per cent basophils and 2 per cent myelocytes. Histologic examination of a specimen removed from the thigh by Dr. G. F. Machacek showed a practically normal epithelium, with only an occasional light sprinkling of polynuclear and round cells. In the corium there were accumulations of lymphocytes and monocytes and some polynuclear cells, which showed a tendency to be gathered in foci around dilated capillaries. The focal nature of these cells was not always sharp. The subcutis was normal. Histologic examination did not support a diagnosis either of dermatitis herpetiformis or of pemphigus but showed a chronic inflammatory reaction in the skin.

The treatment has consisted of bland local applications, intravenous administration of calcium, vitamin therapy and a high caloric diet. There was some improvement until a month ago. After an exacerbation of the eruption at that time, the patient was given sulfanilamide, which produced moderate improvement.

DISCUSSION

DR. CHARLES WOLF: There have been two tentative clinical diagnoses so far. To my mind the man has pemphigus. He has all the characteristics of pemphigus foliaceus and of the bullous type. There is no itching, and he is fairly comfortable.

DR. HOWARD FOX: This patient has recently been in the wards of the Bellevue Hospital for a number of months. My associates and I were uncertain as to the diagnosis. The eruption suggested pemphigus, but the duration was rather long for this disease, and the man did not appear to be ill. I cannot agree with the presenter that the condition has improved, as the eruption is somewhat more extensive than it was when I last saw the patient.

DR. HARRY C. SAUNDERS: This patient came to the Bellevue Hospital during the latter part of February or the early part of March of this year. He had an eruption which all the staff thought was dermatitis herpetiformis. At that time there was intense itching. The condition improved with fever therapy. The fever was induced by typhoid vaccine, given in the manner already described by Dr. Bloom.

A Case for Diagnosis (Lupus Erythematosus? Dermatitis Herpetiformis? Pemphigus?). Presented by DR. JOSEPH J. ELLER.

M. M., a woman aged 65, presents an eruption which began on the abdomen seven months ago and which has gradually beome generalized. It appeared on the face four months ago. Pruritus is marked at times, but the patient complains of no definite pain. At the time of admission to the New York City Hospital, about six weeks ago, she presented an eruption on the entire trunk, the extremities and the face. The lesions consisted of discrete well defined erythematous macules and papules, varying in size from that of a dime to that of a quarter. Slight scaling is apparent at times. There have been no bullae during the period of observation, and the mucous membranes and the orifices of the body have not been involved. On the face the lesions have become confluent to form the large, well defined erythema which she now presents. General physical examination shows no abnormality except dental caries and a large cyst on the right side of the forehead.

The Wassermann reaction was negative, and urinalysis and chemical examination of the blood showed no abnormality. The blood count showed 84 per cent hemoglobin, 5,900,000 red blood cells, 12,400 white blood cells and a differential count of 44 per cent polymorphonuclear leukocytes, 30 per cent lymphocytes, 2 per cent monocytes and 2 per cent eosinophils. Histologic examination by Dr. G. F. Machacek showed a light sprinkling of polynuclear cells and a few round cells in the epithelium. These tended to lie in small clumps to form small intra-epithelial abscesses. The cells of the rete Malpighii tended to be separated by edema in a few areas, and there was an occasional intra-epithelial bleb filled with fluid and

detritus. The corium was sprinkled with polynuclear cells, lymphocytes and monocytes, gathered frequently in foci around engorged capillaries. In the deeper layers of the corium and the subcutaneous tissue a few polynuclear cells were lightly sprinkled in between the bundles of connective tissue. There were few eosinophils. The diagnosis was acute and chronic dermatitis.

DISCUSSION

DR. EUGENE F. TRAUB: This patient's eruption, I believe, conforms in every respect to the so-called Senear-Usher type of pemphigus or bullous lupus erythematosus. No points that I was able to note suggested the diagnosis of dermatitis herpetiformis, nor do I believe that the condition is an ordinary type of lupus erythmatosus.

DR. FRED WISE: I should like to agree with Dr. Traub's diagnosis of pemphigus of the Senear-Usher type. Whenever a patient has persistent lesions on the face which resemble lupus erythematosus or seborrheic eczema, distributed in a butterfly fashion, and small bullous lesions on the body which at one time resemble seborrheic eczema, at another time impetigo contagiosa and perhaps at another time dermatitis herpetiformis, a diagnosis of the Senear-Usher type of pemphigus is to be seriously entertained. Unfortunately, histologic examination does not help much in this type of case. Histologic examination of the lesions on the face probably would not show anything suggestive of pemphigus, but a series of cases of this type have been described in which the lesions on the face showed characteristics of lupus erythematosus while the lesions on the body consisted of small bullae or vesicles. The typical histologic changes of lupus erythematosus and pemphigus do not usually appear, so that the diagnosis must be made on clinical grounds, based on the combination of lesions which the patient shows at one time, as this patient does tonight. Continued observation may result in one of two diagnoses, either bullous lupus erythematosus or a type of pemphigus.

Lichen Sclerosus et Atrophicus (Hallopeau). Presented by DR. DAVID BLOOM.

K. F., a woman aged 60, was previously presented before this section on Jan. 5, 1937 (ARCH. DERMAT. & SYPH. **36**:880 [Oct.] 1937). She is presented again in order to show the marked improvement in the lesions. They are flat, and most of them do not show any follicular roughness. Several lesions on both shoulders show distinct superficial scarring.

The patient has received only solution of potassium arsenite, administered in a dose of 3 minims (0.2 cc.) three times a day, for several months.

Lichen Planus with Unusual Features. Presented by DR. CHARLES WOLF.

H. G., a man aged 38, is presented from the Mount Sinai Hospital because of an eruption of three months' duration, involving the upper and the lower extremities, the genitalia, the mouth, the tongue and the vermilion border of the lips. The eruption consists of two types of lesions: large erythematous, scaly, papular plaques confined to the forearms and arms and discrete papules on the trunk, the palms and the soles. The buccal mucous membrane shows extensive involvement, as does the vermilion border of the lips. The finger nails are discolored and show superficial longitudinal striations. A few bullous lesions are present on the backs of the fingers.

The unusual features are the involvement of the nails, some bullous lesions, the lesions on the palms, the involvement of the buccal mucous membranes and the lesions on the genitalia.

The Wassermann reaction was negative. The blood count showed 102 per cent hemoglobin, 5,800,000 red blood cells, 8,000 white blood cells, 70 per cent polymorphonuclear leukocytes and 27 per cent lymphocytes.

DISCUSSION

DR. EUGENE TRAUGOTT BERNSTEIN: What is the correct diagnosis, lichen planus pemphigoides or lichen planus bullosus?

DR. E. WILLIAM ABRAMOWITZ: Has this eruption been resistant to the ordinary treatment so that it requires a special type of treatment?

DR. EUGENE F. TRAUB: Perhaps one of the most unusual features in this case is the condition to be noted on the mucous membranes. In addition to the slightly elevated glistening, milky white striations or annular rings commonly seen on the mucous membranes in this disease, the patient presents an unusual amount of superficial erosion, which I believe occurs rarely. In fact, I usually look particularly for superficial erosion or ulceration and, if that is present, feel that that rather suggests leukoplakia as against lichen planus. Of course, in this patient the typical lesions of lichen planus elsewhere on the body amply substantiate the diagnosis of lichen planus, despite the usual oral findings.

DR. DAVID L. SATENSTEIN: I object to the term lichen planus of the nails. There is no such dermatosis. It should be lichen planus of the nail bed or lichen planus of the nail bed affecting the nail.

DR. FRED WISE: I believe this is a good opportunity to find out from Dr. Frei, who has had a great deal of experience in Germany, whether he knows of any beneficial results in lichen planus from roentgen treatment of the vertebral column.

DR. WILHELM FREI (by invitation): I have had no experience with spinal irradiation for lichen planus, having employed local irradiation. With this I have had good results. Several times I have seen the involvement of the nails which this patient presents. There is a publication by M. Friedmann, of Jadassohn's clinic, describing cases of this kind.

DR. E. WILLIAM ABRAMOWITZ: I believe it is difficult to draw conclusions from any form of treatment for a disease like lichen planus, which is apt to be resistant and is subject to periods of remission and relapses. After Pautrier introduced the radicular method of roentgen therapy, my associates and I used this treatment in some cases but gave it up as of doubtful value.

DR. ANTHONY C. CIPOLLARO: My associates and I have used the radicular method in some cases of lichen planus at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. My impression is that there was improvement in few. Pautrier in France and Foerster in this country have used this method and have reported good results. We have treated psoriasis by radicular roentgen therapy, and the results have not been too encouraging.

DR. CHARLES WOLF: When first seen, this patient had a few bullae on the fingers, and there were several unusual features, such as large plaquelike areas on the arms and extensive involvement of the mucous membranes of the mouth and of the vermilion border of the lips. The nails show thickening and longitudinal ridges. In answer to Dr. Bernstein, I did not call this condition the pemphigoid type because bullous lesions were not predominant. Treatment has not been started.

A Case for Diagnosis (Pemphigus Foliaceus? Exfoliative Dermatitis?).
Presented by DR. JOSEPH J. ELLER.

D. S., a woman aged 39, states that there has been no illness in her family and that she has had none with the exception of typhus twenty-two years ago. She says that she has had no venereal disease. There is no history of medication or of allergic manifestations. Her eruption began in May 1936, with round red lesions on the external surfaces of the arms. These soon appeared on the legs, and a generalized eruption consisting of "blisters," which later ruptured, then followed.

In July 1937 the patient was admitted to the Bellevue Hospital, where she received potassium permanganate baths and application of mild ointments and

was given seven intravenous injections of germanin, the dose being started at 0.1 grain (0.006 Gm.) and increased to 0.5 grain (0.032 Gm.). The basal metabolic rate was normal and two determinations of the chloride content of the blood gave results of 478.5 and 528 mg. per hundred cubic centimeters. Her condition remained unchanged. On Aug. 27, 1937, she was transferred to the New York City Hospital. At this time she presented a generalized, heavily scaling exfoliation which seemed hyperkeratotic and gave no evidence of bullae or lesions on the mucous membranes. Her temperature varied from 98 to 101.8 F. No actual bullae or lesions in the mouth have been observed since her admission to the New York City Hospital.

The blood count showed 64 per cent hemoglobin, 3,600,000 red blood cells, 10,000 white blood cells, 55 per cent polymorphonuclear leukocytes, 36 per cent lymphocytes, 7 per cent eosinophils and 2 per cent basophils. The Wassermann reaction was negative. Urinalysis showed no abnormality except a 1 plus reaction for albumin. Gastric analysis showed 24 per cent free hydrochloric acid and 40 per cent total hydrochloric acid. Histologic examination of a specimen removed from the leg by Dr. G. F. Machacek showed signs of chronic dermatitis and no specific indications of pemphigus. The epithelium showed slight edema. In it there were a few round and polynuclear cells and a few eosinophils. Mitotic figures were somewhat more numerous than usual in the rete malpighii. The corium contained many poorly delimited areas showing marked edema and heavily infiltrated with lymphocytes, monocytes, a few polynuclear cells and eosinophils and an occasional plasma cell. Between these areas, however, there was some fibrous condensation. There were many chromatophores in the corium. There were no areas of bleb formation. The subcutis was normal.

The patient has received a diet high in calories and vitamins and supplemented with cod liver oil and malt extract, starch baths and mild local applications. Since Aug. 9, 1937, she has been receiving sodium thiosulfate, liver and iron. From August 21 to September 29 she was given 10 grains (0.65 Gm.) of sulfanilamide three times a day. This was discontinued because of chills and possible toxicity.

DISCUSSION

DR. HOWARD FOX: This patient was recently treated in the Bellevue Hospital. At the time of admission she presented a bullous eruption characteristic of pemphigus vulgaris. She had lost weight and had moderately severe constitutional symptoms. The phytopharmacologic test gave results within the limit of toxicity said to indicate pemphigus. After a few months the type of eruption changed to a universal exfoliating dermatitis. As some oozing was associated with the scaling, the diagnosis of pemphigus foliaceus was made. This type of pemphigus is unquestionably rare in the United States, but for some unknown reason it appears to be more common in Brazil. A few years ago I observed six cases of pemphigus foliaceus in one ward in the Santa Casa Hospital in Sao Paulo, Brazil.

A Case for Diagnosis (Neurodermatitis?). Presented by DR. JOSEPH J. ELLER.

J. S., a man aged 43, has had an eruption since his childhood, with periods of remission and exacerbation. There is no history of allergic manifestations. He was previously hospitalized at the New York City Hospital and discharged in October 1936, with a small pigmented lesion on the face. He worked on a farm after that, and a generalized papular eruption developed on the face, the upper and lower extremities, the scrotum and the buttocks. The skin always becomes lichenified and pigmented and is intensely pruritic.

A roentgenogram of the chest showed no abnormalities. The Wassermann reaction was normal. Chemical examination of the blood showed nothing abnormal, the sugar content being 114 mg. per hundred cubic centimeters. The electrocardiogram showed chronic auricular fibrillation and a pulse rate of 82 per minute.

Urinalysis showed no abnormality. The blood count showed 60 per cent hemoglobin, 3,800,000 red blood cells and 8,800 white blood cells, with a normal differential count. Several carious teeth were extracted.

Previous therapy had consisted of application of mild ointments and 10 per cent juniper tar in paste of zinc oxide N. F. (Lassar's paste) and potassium permanganate baths. From June 8 to June 24, 1937, the patient received ultraviolet irradiation every three days. He was placed then in the fever therapy machine once a week and the temperature raised beyond 104 F. for nine treatments. He has received a high vitamin diet, intramuscular injections of liver extract and vitamin C and twenty injections of calcium thiosulfate.

Histologic examination of a specimen of skin removed from the thigh by Dr. G. F. Machacek showed chronic and acute dermatitis. The squamous epithelium showed possible acanthosis, but this was mild. In a few areas it was definite, and there were a few discrete, widely separated rete pegs which showed marked hyperplasia and down growth. There was an occasional small purulent focus in the epithelium and close by an occasional small intra-epithelial bleb containing some serous material. The pars papillaris of the corium contained several small, loose, edematous accumulations of lymphocytes and monocytes and an occasional eosinophil. These foci were usually discrete, but between them were some sprinklings of similar inflammatory cells. The deeper part of the corium and the subcutaneous tissue were normal. Most of the sweat glands and hair follicles were normal, but around an occasional sweat gland was a cellular focus similar to those found in the corium.

DISCUSSION

DR. HOWARD FOX: Has an examination for amyloid been made?

DR. DAVID L. SATENSTEIN: I believe this case fits in with those that Drs. Rosen and Sulzberger have been talking about recently. Dr. Sulzberger and his associate reported a series recently in the ARCHIVES (Sulzberger, M. B., and Garbe, W.: Nine Cases of a Distinctive Exudative Discoid and Lichenoid Chronic Dermatosis, ARCH. DERMAT. & SYPH. **36**:247 [Aug.] 1937). There is no definite name for this dermatosis. It presents various pictures, of neurodermatitis, of weeping eczema, of mycosis fungoides and so on. Patients with this condition go through various remissions, getting better and getting worse. A number of cases have been presented before this section in which the picture would fit in with this type of dermatosis. They have been presented under such labels as neurodermatitis, allergic dermatitis, ordinary eczema and mycosis fungoides.

DR. JOSEPH J. ELLER: I agree with Dr. Satenstein's interpretation. Examination for amyloid, as suggested by Dr. Fox, will be made and reported on at the next meeting.

A Case for Diagnosis (Lymphogranuloma Venereum?). Presented by DR. JOSEPH J. ELLER.

L. U., a man aged 53, first noticed a lesion on the penis in June 1937. He received ten intramuscular and four intravenous injections while under treatment in the Kings County Hospital, Brooklyn. There is no record of a dark field examination or a Wassermann test at this hospital. The lesion enlarged during treatment, and the patient was admitted for a dorsal slit operation. He was transferred to the New York City Hospital on Oct. 1, 1937. Examination showed moderately enlarged, discrete nontender inguinal lymph nodes. The Wassermann reaction was 4 plus. Dark field examination, smears for Ducrey bacillus and Donovan bodies and the Frei test gave negative results.

DISCUSSION

DR. WILHELM FREI (by invitation): I think this condition is not serpiginous chancroid. Serpiginous chancroid advances with intensive cicatrization and emanates usually from a bubo. I believe it is granuloma inguinale. The members

have observed, I believe, five cases of granuloma inguinale this evening, and in none of them could Donovan bodies be found. It is often difficult to find these bodies.

DR. LOUIS TULIPAN: I understand that this case came under observation only today. I cannot understand then how the examination of a piece of tissue for Donovan bodies could have been made. The man did not say he had any tissue removed. I want to mention the fact that all the members have had difficulty in finding the Unna-Ducrey bacillus in chancroid. At the Bellevue Hospital, since my associates and I have been producing auto-inoculated lesions on the arm, we have not had any difficulty in finding the bacillus there. It has been found easily in the lesions on the arm.

DR. LOUIS CHARGIN: In a considerable number of cases of ulcer of the genitals in which syphilis could be ruled out or in which there was a mixed infection, I have been able to find the Unna-Ducrey bacillus with the Unna-Pappenheim stain. It is superior to any other which I have employed for the purpose. By the use of this stain it has been possible to find the Unna-Ducrey bacillus in about 20 per cent of nonsyphilitic ulcers.

DR. DAVID BLOOM: At the Bellevue Hospital in the diagnosis of chancroid autoinoculation is of great help—perhaps more valuable than intradermal inoculation with Ducrey vaccine, because the latter may indicate a past chancroid infection. By autoinoculation one may be fairly sure that the present condition is chancroid.

DR. G. F. MACHACEK: I should not be disturbed because Donovan bodies were not found in one or two smears. In cases like this it is not always possible to find them unless repeated examinations are made. I think the examination of smears is a better method than examination of sections of tissue. I do not believe it makes much difference what stain is used. It is necessary to scrape under the undermined border for the specimen. There are too many other organisms in the slough. These lesions are small. That is probably why the autoinoculated lesions give better results, because they are larger. Methylene blue is just as effective as any other stain.

DR. DAVID L. SATENSTEIN: I should like to bring up the question of possible epithelioma developing on the dorsal slit, due to arsenical treatment. The patient states that the lesion appeared after the treatment had been started.

Ulcerating Gumma of Unusual Size. Presented by DR. HOWARD FOX.

C. M., a man aged 61, was admitted to the Bellevue Hospital on Aug. 12, 1937. He stated that he had a penile sore in 1898, which was followed by a generalized rash. He was treated at that time with mercurial inunctions. Seven months prior to admission the patient sustained an injury to his left shoulder, and for the following two months he complained of moderate pain in the left scapular region. Subsequently there were no local signs or symptoms, until two weeks before admission, when the present lesion was first noticed. It grew rapidly but occasioned no constitutional symptoms. At the time of admission he presented a necrotic mass the size of a grapefruit, which caused only slight pain and tenderness. It measured 7.5 by 18 cm. Within a week necrotic sloughs separated, leaving a large ulcer which has steadily diminished under antisyphilitic treatment.

DISCUSSION

DR. DAVID BLOOM: When the patient was first seen, two diagnoses were considered, gumma and carbuncle. The relative indolence of the lesion, the good general condition of the patient, the lack of fever and the lack of marked inflammation around the lesion suggested gumma rather than carbuncle. Treatment with iodide and a bismuth preparation has made the large tumor, which consisted of necrotic tissue, disappear. The lesion is now in the stage of reparation, and therefore a definite diagnosis cannot be made from the present picture.

DR. HOWARD FOX: Although there can be no doubt that the present lesion is a healing gummatous ulcer, it presents a somewhat quadrangular appearance suggesting a factitious lesion. The patient was observed, however, before the tumor broke down and ulcerated, and any factitious element may therefore be excluded.

Elephantiasis of the Penis Associated with Granuloma Inguinale. Presented by DR. HOWARD FOX.

F. D., a full blooded Negro aged 27, a laborer, has always lived in Maryland except for occasional trips to Miami, Fla., and one trip to Philadelphia in the fall of 1935, where he spent two and a half months. In 1932 he had "very tender glands" in the right groin, which disappeared spontaneously after several months without breaking down. In the fall of 1934, while in Miami, he noticed two small, painless sores on the penis, one on the foreskin and one on the undersurface of the shaft, near the scrotum. The lesions were not treated until December of that year, when he contracted gonorrhea. This was associated with a good deal of swelling of the foreskin. A local physician told him he had gonorrhea and a "chancre or chancroid" and performed circumcision. About two months later the lesion at the root of the penis began to enlarge, and the entire penis began to swell, this process having continued up to the present time. The patient now presents extreme elephantiasis of the entire penis, which measures 40 cm. in circumference. There is an ulcer 11 cm. long and varying in width from ½ to 1 inch (1.3 to 2.5 cm.) near the base of the penis and extending about two thirds of its circumference. It is beefy red and has a slightly elevated rolled border and an uneven base, with a number of small elevated granulomatous masses. There is no regional adenopathy. There are several similar small ulcerations on the margins of the skin surrounding the glans. The Wassermann reaction was 4 plus and the Frei reaction positive. The Dmelcos test gave strongly positive results, but autoinoculation for chancroid gave negative results. No Donovan bodies were found in smears from the ulcers.

DISCUSSION

DR. WILHELM FREI (by invitation): The picture of elephantiasis in this case would correspond more with lymphogranuloma venereum than with granuloma inguinale. On the other hand, elephantiasis of the penis in association with lymphogranuloma venereum and without preceding involvement of the inguinal glands is rare. The patient has had no involvement of the inguinal glands. At the same time, the luxurious exuberance of the ulcers corresponds more with granuloma inguinale. Altogether, I should believe that this case, in spite of the positive reaction for lymphogranuloma venereum, is rather one of granuloma inguinale.

DR. DAVID BLOOM: In the European literature one reads that lymphogranuloma venereum is often associated with elephantiasis of this type. This association is rarely seen here in the United States. More frequently the association is with granuloma inguinale. In the last year there was presented at the Academy of Medicine a case of granuloma inguinale accompanied with marked elephantiasis of the scrotum, in which the penis was buried. I observed another case of granuloma inguinale, in a woman. There was associated extreme elephantiasic enlargement of the abdominal wall. I believe, therefore, that elephantiasis is more frequently associated with granuloma inguinale than with lymphogranuloma venereum.

DR. FRED WISE: I should like to ask Dr. Fox whether he has excluded Filaria bancrofti.

DR. T. J. RIORDAN: It is not amiss to repeat previous statements about examinations for Donovan bodies. This case well illustrates how the Donovan bodies may be missed. If a piece of fibrous tissue is examined Donovan bodies cannot be found. Symmers called attention to the fact that the correct way to search for the Donovan bodies is by biopsy, taking the specimen as near as possible to a pus

pocket, and spreading material from the deep side of the biopsy tissue. Examination should be made of at least forty slides, not two or three slides. Another method, of course, is by examination of direct smears. Then a sharp instrument, such as a curet or a razor blade, should be used.

DR. HOWARD FOX: I think the ulcerated areas are typical of granuloma inguinale and that the elephantiasic condition is probably associated with this disease. In an analysis of the American literature on granuloma inguinale a number of years ago I found fourteen cases of elephantiasic enlargement of the genitals in a total of one hundred and fifty cases. This patient, however, presents the most striking picture of elephantiasis of the penis which I have ever seen. I do not think the positive Frei and the positive Wassermann reaction are significant in this case. Following Dr. Wise's suggestion, I shall make a search for Filaria, though this man has apparently not lived in a region where filariasis is endemic. Furthermore, the scrotum is not involved.

A Case for Diagnosis (Sycosis Vulgaris? Tinea Barbae?). Presented by DR. GEORGE M. LEWIS.

W. L., a man aged 22, who handles silks, states that an eruption developed on the left cheek four months ago. This has slowly enlarged, and smaller lesions have appeared. The largest patch on the left cheek shows a boggy infiltration from which hair can be epilated without much pain. There are a few follicular pustules. There is no history of contact with animals. Examination for the presence of fungi on two occasions gave negative results. Histologic examination showed chronic eczema.

DISCUSSION

DR. GEORGE M. LEWIS: Every one will probably agree that this condition has the clinical appearance of a fungous infection. So far, fungi have not been demonstrated in a smear or culture. Dr. Goodman suggested informally the possibility of drug eruption, since he elicited a history of ingestion of several proprietary drugs.

DR. CHARLES WOLF: At first glance you might think this condition is a fungous infection. The patient gives a history which is interesting of having had applications of radium bromide to the lesion. It might well be that he has radium dermatitis superimposed on the original infection.

DR. E. WILLIAM ABRAMOWITZ: Anacin, which the patient has taken, contains acetophenetidin, acetylsalicylic acid, quinine and caffeine. I do not believe any of these drugs would cause this eruption. Clinically, this condition gives me the impression of a fungous infection. Perhaps the marked reaction has been responsible for the fact that no fungi have been found so far.

A Case for Diagnosis (Syphilis? Tuberculosis?). Presented by DR. JOSEPH J. ELLER.

E. W., a man aged 51, presented from the New York City Hospital, first noticed an ulcer on the left leg three month ago. At the age of 10 years he had "rheumatic fever" and at the same age a "piece of bone" was removed from each leg. He states that he has had no venereal disease. Examination shows on the left thigh and leg three fungating ulcers surrounded by parchment-like scar tissue with a darkly pigmented border. There are numerous other scars on the other extremities and in the right clavicular region (from previous incision?).

Physical examination showed irregular pupils, which reacted well in accommodation but sluggishly to light. The blood pressure was 160 systolic and 100 diastolic. The Wassermann reaction of the blood was repeatedly 4 plus. Examination of the spinal fluid gave negative results. The reaction to the Mantoux test was 2 plus. Chemical examination of the blood and urinalysis showed no abnormality. The blood count was essentially normal. Roentgenograms of the

long bones showed moderate diffuse sclerosing osteomyelitis of the shafts of both femurs but no demonstrable evidence of an acute breakdown within the bone; the long bones of the legs and of the right upper extremity were normal. The outer half of the right clavicle was distorted, and the medial half was completely absent, probably the end-result of an acute inflammatory process during which the medial half of the bone was either destroyed or removed. A roentgenogram of the chest showed a thickening of the apical pleura on the right side, the remainder of the lung fields being essentially normal.

Histologic examination of a biopsy specimen showed chronic and acute inflammation and a foreign body reaction. The epithelium was fairly normal in some areas and showed acanthosis and edema in other areas, with a sprinkling of polynuclear and round cells and some edematous, disorganized rete pegs projecting into the corium. In some places there was almost complete destruction by polynuclear cells, leaving only a thin overlying margin of keratinized material. The corium and the subcutaneous tissue, down to the lower edge of the specimen, showed profound edema, vascular dilatation and a heavy cellular infiltration of plasma cells, polynuclear cells, eosinophils, lymphocytes and monocytes. Plasma cells were predominant. There were focal accumulations of both round and polynuclear cells, the latter forming small abscesses. In the subcutaneous tissue were some small collections of Langhans giant cells, surrounded by round cells, chiefly lymphocytes. The giant cells contained an occasional highly refractile or deep blue staining (calcific?) foreign body. The small vessels showed endothelial swelling but no endarteritis.

The patient had received three injections of neoarsphenamine and two injections of a bismuth preparation before his admission to the New York City Hospital. Since his admission he has had two injections of arsphenamine and one of a bismuth preparations. Potassium permanganate and strong mercurial ointment have been applied to the lesions.

DISCUSSION

DR. FRANK C. COMBES: I should like to know if any one here thinks this condition is syphilis.

DR. LOUIS TULIPAN: I should make a diagnosis of syphilis if only because of the scars on the upper third of the left leg, that being the usual location for syphilitic lesions.

DR. HOWARD FOX: I think the evidence favors tuberculosis in this case, partly because of the associated changes in the lungs and the bones. The cutaneous lesions are not as sharply defined as they usually are in syphilitic nodules or gummas; furthermore, there are numerous active lesions in spite of an adequate therapeutic test with neoarsphenamine and a bismuth preparation. The small pliable scars which were considered by one of the members to be indicative of syphilis were stated by the patient to have been the site of skin grafts.

DR. LOUIS TULIPAN: I asked the patient, and he said he had had some ulcers on the leg which had healed. If those were ulcers, I should make the diagnosis on the basis of the location of the scars.

DR. A. W. GRACE: The patient told me those were the sites of skin grafts.

DR. JOSEPH J. ELLER: I think it is possible that the condition is tuberculosis in a syphilitic patient.

Osler's Disease (Hereditary Familial Telangiectasia). Presented by DR. DAVID BLOOM.

C. D., an Italian man aged 50, is presented from the Bellevue Hospital. Since the age of 5 years he has had nosebleeds, which have often necessitated hospitalization. He never had any difficulty with bleeding from cutaneous wounds. He presents numerous telangiectatic lesions of the size of a pinhead and somewhat larger on the lips, the face, the palate and the tongue. His father, three brothers,

one sister and other members of the family are affected with the same condition. In four generations, five women and nine men out of forty-three members of the family have been similarly affected.

The blood count showed 4,300,000 red blood cells, 64 per cent hemoglobin, 7,050 white blood cells and a differential count of 76 per cent polymorphonuclear leukocytes, 23 per cent lymphocytes and 1 per cent eosinophils on one occasion. On another occasion there were 5,400,000 red blood cells, 63 per cent hemoglobin, 6,850 white blood cells, 74 per cent polymorphonuclear leukocytes, 19 per cent lymphocytes, 6 per cent eosinophils and 1 per cent basophils. The clotting time was seven and one-half minutes, the bleednig time five and one-fourth minutes and the blood platelet count 170,000. The blood pressure was 102 systolic and 34 diastolic.

Naevus Pigmentation et Pilosus. Presented by DR. HENRY D. NILES.

Lupus Vulgaris. Presented by DR. G. D. ASTRACHAN.

A Case for Diagnosis (Granuloma Inguinale?), Showing Marked Improvement Under Roentgen Therapy. Presented by DR. JOSEPH J. ELLER.

A Case for Diagnosis (Chancroid?). Presented by DR. JOSEPH J. ELLER.

Chancre and Chancroid (Granuloma Inguinale?). Presented by DR. JOSEPH J. ELLER.

A Case for Diagnosis (Chancre? Chancroid?). Presented by DR. JOSEPH J. ELLER.

A Case for Diagnosis (Granuloma Inguinale?). Presented by DR. JOSEPH J. ELLER.

Granuloma Inguinale. Presented by DR. JOSEPH J. ELLER.

A Case for Diagnosis (Allergic Dermatitis?). Presented by DR. JOSEPH J. ELLER.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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Oct. 15, 1937

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Lupus Erythematosus (Sarcoid Type of Tuberculosis Cutis in the Negro). Presented by DR. CARMEN CHRISTINE THOMAS, Wilmington, Del. (by invitation), from the Dermatologic Clinic, University of Pennsylvania Hospital.

A. D., a Negress, aged 31, presents on the vertex of the scalp three or four atrophic, scarred bald areas. Over the malar regions of the face, the chin, the eyelids, the nasal septum, the vermilion borders of the lips, the pinnae of the ears and the retro-auricular regions are variously sized flat, round or oval discrete and confluent plaques and papules. Most of them show a hyperpigmented depressed center. Many show in addition a dusky erythematous elevated border. The recent lesions in the suprasternal notch are annular and look like eroded vesicles.

The mucous membranes are normal. The inguinal and submaxillary nodes show shotty enlargement. The teeth are carious and the gums spongy and inflamed. The patient has had the same type of lesions on the face periodically since early childhood. Previously the eruption has always flared in the summer and subsided during the winter. Urinalysis showed albumin and from 35 to 40 pus cells per high power field. The Kolmer and the Kahn test gave weakly positive results, and the reactions to tuberculin tests were negative.

DISCUSSION

DR. JOSEPH V. KLAUDER: The case impresses me as one of common lupus erythematosus.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I do not understand the deep atrophy in this case. It impressed me as probably a real type of tuberculosis of the skin rather than lupus erythematosus.

Moniliasis. Presented by DR. W. R. HILL (by invitation) for DR. JOHN H. STOKES.

M. M., a white woman aged 45, presents on the scalp brownish diffuse areas apprarently due to poor hygiene. There are reddish circular pea-sized scaling macules at the angles of the mouth. Anterior to the left ear on the left cheek, on the dorsum of the right hand and the dorsum of the left large toe, beneath the right breast and about the umbilicus there are oval reddish discrete macules varying in size from that of a pea to that of a silver dollar with smooth, shiny surfaces and well defined borders. Several have a yellowish, slightly adherent scale. About the perineum and the gluteal fold the patches, which are confluent, appear symmetrically apposed. There is moderate infiltration. There are white macerated areas between the toes. The primary lesion is a reddish papule that gradually extends peripherally. The patient first noted the eruption at the angle of the mouth one year ago. The pruritus is most marked at night, interfering with sleep. The eruption has never entirely cleared. The Kolmer modification of the Wassermann test and the Kahn test gave negative results. Examination of scales from the gluteal crease showed no fungi. Culture of material from this area showed yeast. The reaction to oidiomycin was 2 plus and that to trichophytin negative.

DISCUSSION

DR. D. M. SIDLICK: Laboratory investigation may support the diagnosis of moniliasis, but on the clinical evidence I believe this case to be one of psoriasis.

DR. FRED D. WEIDMAN: There are psoriasiform types of dermatophytosis. I think the predominantly intertriginous tendency of this eruption would warrant, on clinical grounds, the diagnosis of a fungous infection of some sort. The cultures that are shown, I think, are those not of a yeast but of a bacterium; however, I think the preponderance of the evidence is in favor of a yeast infection.

Prurigo Nodularis. Presented by DR. BERTRAM SHAFFER (by invitation), from the Dermatologic Clinic, University of Pennsylvania Hospital.

R. J., a Negress, aged 22, presents on the extremities an eruption consisting of fibrotic papules and nodules, many of which are capped by a keratotic and slightly verrucous mass. Some of the lesions are disposed in linear configuration as if they had formed on scratch marks. They are most profuse and best developed on the extensor surfaces of the limbs. The patient states that the eruption began as "hives" in the early summer of 1935 and has persisted with almost no change. Subjectively there is extreme paroxysmal pruritus at the site of each lesion, usually more marked at night. The Kolmer and the Kahn test were negative. A lesion on the thigh was removed on Aug. 18, 1937, and its histologic features were reported by Dr. Herman Beerman as compatible with the

diagnosis of prurigo nodularis. Since Aug. 29, 1937, the patient has received biweekly injections of solution of parathyroid (50 units each) with no relief of pruritus or involution of the eruption.

DISCUSSION

DR. FRED D. WEIDMAN: I think that prurigo nodularis is the most probable diagnosis. The eternal question of whether lichen obtusus corneus and prurigo nodularis are the same must be considered on an occasion of this sort. I strongly doubt that a distinction can be made between these two conditions on a histologic basis.

DR. JOSEPH V. KLAUDER: According to my conception, the lesion of prurigo nodularis is a definitely thickened, cornified nodule with a rough verrucous surface. This patient does not have that type of lesion. Whether she will eventually present it I do not know. One cannot say that this condition is typical.

DR. CARROLL S. WRIGHT: I feel that this condition readily comes under the classification of prurigo nodularis. If a patient with that disease does enough scratching, he can keep the verrucous element pretty well down. I think the lesions on the legs of the patient tonight are typical.

DR. FRED D. WEIDMAN: At one time I destroyed two or three such lesions with solid carbon dioxide, and to my amazement many of the other lesions spontaneously disappeared.

DR. ABRAM STRAUSS: It seems to me that this patient presents many features of true lichen planus on the arm, with typical linear arrangement of lesions. In the mouth I saw a lichen planus lesion, and the patient altogether impressed me as having long-standing lichen planus rather than prurigo nodularis.

DR. JOHN H. STOKES: One thing which interests me here is the linear arrangement; when five, six or seven lesions occur at intervals on a leg, it is hard to believe that the involvement is all due to scratching. There is a variety of lichen planus, the so-called moniliform type (lichen ruber moniliformis), which is one of the extreme rarities in dermatologic practice. I think lichen planus with a moniliform tendency should be brought into the diagnosis of this case.

DR. DONALD M. PILLSBURY: The possibility of lichen planus has been continuously considered in this case. The lesions on the flexor surfaces and the wrist when examined under the lens in daylight do not show the characteristics of lichen planus and are keloidal. No lesions have ever been noted in the mouth, although the mucous membranes have been examined repeatedly. The diagnosis presented seems to be the most logical one.

DR. ABRAM STRAUSS: I suggest the trial of mercury intravenously in this case. I have seen remarkable relief of itching in lichen planus, ordinary and hypertrophic, following the use of mercuric benzoate or mercuric cyanide intravenously.

A Case for Diagnosis (Neurodermatitis?). Presented by DR. FREDERICK EARLE KUNKEL, West Hartford, Conn. (by invitation), from the Dermatologic Clinic, University of Pennsylvania Hospital.

S. W., a white boy aged 11 years, is well developed and slightly undernourished and shows slight mental and muscular sluggishness. The skin on the palms and the soles is uniformly thickened, rough, dry, hard and yellowish brown. There are fissures at various places on the soles. The hyperkeratosis ends abruptly at the margins of the feet. On the joints of the toes, the fingers, the wrists, the ankles and the dorsum of each foot are plaques of hyperkeratotic skin varying in diameter from 1 to 2 cm. Over the extensor surfaces of the elbows and the knees the skin is dry, thickened and scaling. Close examination shows numerous minute scaly papules, many of which are topped by a central horny plug. In the horny centers hairs can be seen protruding. On the dorsum

of each index finger are papules, some of which are acuminate, pinhead size, skin colored and topped by a central horny plug. On the extensor surfaces of the extremities, the shoulders, the nucha, the ears and the face are small oval, irregular patches of dry thin whitish adherent scales. The nails of the toes are dull, slightly rough and thickened. The entire involvement is generally symmetrical. The skin of the uninvolved regions is normal. The hair is normal and the scalp clean. Three years ago the child first complained of dryness and thickening of the soles. About one month later a similar condition developed on the palms. This condition has gradually progressed. At times improvement has been noted, but never have the symptoms completely disappeared. When the disease is at its height, deep fissures appear on the palms and the soles, which become tender. For one year shortly after the onset of symptoms, 3 drops of a liquid green medicine, prescribed by a physician, was taken three times daily in water. The Kolmer and the Kahn test were negative. The sugar content of the blood on October 1 was 55 mg. per hundred cubic centimeters and on October 6, 80 mg. The cholesterol content of the blood was 166 mg. The basal metabolic rate was —17. The reaction to tuberculin was negative. The chief histologic manifestations were hyperkeratosis, moderate acanthosis, edema of the epidermis and a scant round cell infiltrate in the corium. The changes were most marked around the hair follicles. The patient has been put on a diet high in vitamins and an ointment containing 5 per cent salicylic acid given.

DISCUSSION

DR. JOSEPH V. KLAUDER: The diagnosis of neurodermatitis cannot be excluded by the family history, and I think it should be given consideration.

DR. FRANK C. KNOWLES: I cannot but feel that what Dr. Klauder says is correct. The mother has a patch of neurodermatitis on her arm. Evidently curious factors are at work in the household and the family. I cannot help feeling that this thing developed at an earlier age than the patient states and that, though it might have been comparatively slight, there must have been some symmetrical arrangement on the palms and the soles—not keratoderma palmare et plantare but an inflammatory element which shows itself in the development of keratoderma instead of keratosis. The mild condition which I believe has been present earlier than is stated in the history was excited by an attack of measles and of scarlet fever, and the exacerbation occurred shortly after and then came more to the notice of the mother.

DR. DONALD M. PILLSBURY: I should like to agree with the diagnosis of keratoderma suggested by Drs. Klauder and Knowles. The absence of a history of the disease in the family is not against this diagnosis, and the widespread involvement of the body, particularly of the knuckles and the elbows, is not uncommon.

DR. ROBERT L. GILMAN: I do not believe that a biopsy would exclude a diagnosis of psoriasis. In that connection I believe this case might well represent an example of Dr. Stokes' explanation of the monilial concept of psoriasis. The last word cannot be said in this case until the boy's tonsils receive attention, and I think further studies for organisms on the hands and feet and removal of the tonsils might shed some light on the situation.

DR. DONALD M. PILLSBURY: Can any one suggest any possible therapeutic approach to this problem?

DR. JOSEPH V. KLAUDER: One might study the sulfur balance of the skin, the hair and the nails and if any clues are obtained give the patient one of the amino-acids containing sulfur.

A Case for Diagnosis (Lupus Vulgaris Erythematoides?) in a Patient with Healed Lupus Erythematosus. Presented by DR. REUBEN FRIEDMAN.

E. S., a white woman aged 43, states that lupus erythematosus developed in 1924 and involved the left ear and adjacent areas. In the succeeding six years

many other portions of her face became involved. In 1930, after twelve injections of sodium gold thiosulfate, a widespread purpuric eruption suddenly developed on her limbs and oral mucous membranes. This was associated with severe epistaxis and gingival bleeding and followed by almost fatal hematemesis, hematuria and rectal bleeding. After this episode the patches of lupus, which had previously shown a hemorrhagic purplish discoloration, assumed a somewhat whitish flesh color, which they have retained to date.

In the summer of 1931 small slightly raised reddish acneform papules appeared on the front of her chest and neck. Some of these lesions have undergone suppuration, while in the centers of the others has developed a small, hard, yellowish, tender, splinter-like body. In 1934 several groups of small warty lesions and blackheads appeared on the right side of the chin and spread peripherally. These were surrounded by a reddish, elevated border which contained pinpoint-sized yellowish spots from which could be expressed a cheeselike or purulent substance of unpleasant odor. A biopsy specimen taken in 1936 from one of the lesions on the chest showed "a cystic dilatation of the sweat glands, with heavy lymphocytic infiltration of the coils. The glands themselves were enlarged and edematous and seemed more numerous than normal for the region. The sebaceous glands were less certainly in places not at all involved. There were neither the characteristic plugs of lupus erythematosus nor epitheliomatous changes. There were neither tubercles nor endarteritis." There is now on the right side of the chin an oval, sharply marginated lesion about 6.5 by 5 cm. The border is bandlike, about 1 cm. wide, pale red, dense, elevated and moderately smooth, and here and there under the thin epidermal covering are plainly visible pinhead-sized yellowish bodies with either central depressions or dark, comedo-like centers. A cheesy, ill-smelling, sebum-like material can be expressed. The center of the patch is pale and filled with what seems like a mass of filiform and slightly larger verrucae on a scarred base. No ulceration is present. On the upper lip are three lesions, each about 1.5 cm. in diameter, one of which occupies the upper part of the philtrum. All present a punched-out appearance, with dry, scarred bases and rather irregular jagged borders. An abortive tendency to elevated bandlike margination, as described previously, is present on two of these lesions. On the front of the chest, on the clavicles and on the sides of the neck are numerous discrete, mildly erythematous, slightly raised papules of varying size. They whiten readily under diascopic pressure.

DISCUSSION

Dr. Joseph V. Klauder: The lesion on the right side of the patient's chin and the one above it resemble naevus comedonicus as well as folliculitis ulerythematosa reticulata. I do not believe that it is lupus vulgaris of the Leloir type.

Dr. Fred D. Weidman: The lesions on the chest might be fundamentally tuberculous. It is possible that isolated microscopic tubercles may be occluding the secretory ducts, thus leading to retention cysts of one of the appendages. The distribution on the upper part of the chest is compatible with what is seen in syringoma. The lesions are highly inflammatory, but I can still see where tuberculosis might play a fundamental part in the production of these lesions on the chest.

Dr. Reuben Friedman: I want to call attention to the distinctly inflammatory condition in that border, which includes a number of yellowish bodies apparently containing sebaceous material. I think that this particular picture conforms to that which Ormsby described as Leloir's erythematoid lupus vulgaris. I want to call particular attention to the unusual therapeutic result, so far as the erythematous lupus was concerned, of the attack of acute purpura haemorrhagica secondary to the administration of sodium gold thiosulfate.

Dr. Joseph V. Klauder: The scarring in the lupous type of tuberculosis is smooth and atrophic and not of the retiform or honeycombed type which this patient exhibits.

Secondary Syphilis—Tinea Capitis. Presented by DR. BERTRAM SHAFFER (by invitation), from the Dermatologic Clinic, University of Pennsylvania Hospital.

S. W., a Negro aged 4 years, has had scaling and patchy loss of the hair of the scalp since April 1937. Three weeks ago he became generally ill, and today the present eruption appeared. The child is slightly undernourished but appears generally healthy. A subsiding pigmented maculopapular eruption appears about the face, the neck, the shoulders, the trunk and the upper extremities. A few of the lesions are distinctly annular and present pigmented centers. The scalp is the site of a diffuse, patchy scaling process. Here and there some loss of hair is present. Medical examination showed no abnormality except an injected pharynx and generalized shotty adenopathy. The Kline and the Kahn test were strongly positive. Scrapings and hair stained with potassium hydroxide showed fungi and spores. Examination of serum from one of the lesions on the chest showed motile Spirochaeta pallida.

DISCUSSION

DR. JOSEPH V. KLAUDER: The eruption that this child presents certainly is not the secondary rash of acquired syphilis. The results of clinical and of dark field examination do not agree; so I think the tests should be repeated.

DR. JOHN H. STOKES: I would point out some things that are favorable to the diagnosis of syphilis here. One of course thinks of the mother as having had a positive Wassermann reaction. I looked over the child for evidence of prenatal infection but could no find any. His tibias are perhaps a trifle thick but not enough so to establish a diagnosis. I did not get enough of a grip on the adenopathy to be able to reach a conclusion as to whether the condition presents that rare picture of so-called bubon d'emblée, in which the primary lesion occurs not on the mucous surface but in the adjacent glands, so that a single gland or a group of two or three may constitute the primary lesion. I should say that the finding of S. pallida in a dry lesion on the glabrous skin will have to be considered. These lesions then must be syphilid—the most probable diagnosis—unless the patient has yaws.

DR. JOSEPH V. KLAUDER: If the condition turns out to be acquired syphilis, I think it might be well to consider the possibility of interstitial keratitis. It has been said that interstitial keratitis is likely to occur when syphilis is acquired in childhood. I have never been able to confirm or refute that, because I have not observed enough cases.

Rosacea; Rosacea Keratitis (Tuberculous Keratitis? Lewandowsky's Tuberculid?). Presented by DR. CARMEN CHRISTINE THOMAS, Wilmington, Del. (by invitation), from the Dermatologic Clinic, University of Pennsylvania Hospital.

W. McK., a white woman aged 37, presents marked flushing of the area subject to rosacea, numerous papules of the malar region and pustules of the forehead. At the time of admission there were marked blepharitis, conjunctival injection, corneal haziness and photophobia in the right eye, and the scalp showed evidence of seborrhea. One week later the left eye presented similar involvement. The papules on the face at no time showed apple jelly nodules or infiltration. Occasionally pustules have been noted. About three weeks ago a sharply demarcated erythematous swelling appeared under the right eye, at the point at which the patient's skin comes in contact with the nickel frames of her glasses. There is gingivitis of the lower gum. The face has been flushed for about two years, during which time the menses have been irregular. The Kolmer and the Kahn tests were negative. A roentgenogram of the chest showed no abnormality. A tuberculin test with 0.00002 mg. of Penfield protein derivative (first test dose) showed a 3 plus reaction. Patch tests on Oct. 1, 1937, with a 10 per cent solution of nickel chloride and with a nickel gave positive results. Treatment included oral administration of calcium gluconate, 1 drachm (3.9 Gm.) twice a day, and of dilute hydrochloric acid, 40 drops three times a day; a diet low in carbohydrates;

intramuscular injections of boiled milk for seven weeks and seven injections, 2,000 units each of theelin. After this therapy the right eye was much improved; the left did not improve. The face showed little change. Three injections of 10 mg. of sodium gold thiosulfate were then given, together with roentgen therapy (8 doses of 31 r to the unprotected eyes and 13 doses of 31 r to the sides and the front of the face). A paste composed of resorcinol and sulfur was applied locally, and treatment for the eyes prescribed by the ophthalmologic outpatient department was carried out.

DISCUSSION

DR. JOSEPH V. KLAUDER: The corneal lesion does not look exactly like the keratitis characteristic of rosacea. It is too retiform; it lacks the sharply marginated white appearance of the infiltrate that characterizes rosacea. At the same time the patient has rosacea, and the association of the two, I think, would make rosacea keratitis a reasonable diagnosis.

DR. DONALD M. PILLSBURY: The ocular lesion is much improved at present. Because of a suggestion from the ophthalmologic department that this process of the eye might be tuberculous and of the finding of what seemed suggestive apple jelly nodules in the skin of the face, my associates and I began cautiously to give a gold preparation. It has been my feeling that the improvement in the eye has dated from the inception of that form of treatment.

DR. JOHN H. STOKES: Two things are of interest to me here. One of them is the presence of sensitiveness to nickel in this patient. I think that deserves comment, particularly because of the interplay which seems to exist between sensitiveness to nickel and pyogenic infections. When I have had to deal with sensitiveness to nickel recently I have always taken pains to make a search for pyogenic foci. I think that association is sometimes overlooked in rosacea. The persistence of a single focus of pyogenic infection—an infected tooth or bad tonsils or anything else—will block this woman's improvement. If a furuncle develops, her rosacea will flare up immediately; the sensitiveness to nickel will become more pronounced for a time, and she will lose the ground she has gained. The cure of rosacea keratitis can be furthered—though certainly not completely accomplished—by treating the condition according to the systemic regimen used in rosacea and considering it not as a manifestation of demodectic infection but of hypochlorhydria. I should give her a drachm (3.7 cc.) of dilute hydrochloric acid at first and an hour later give a similar dose. I should follow the routine of the Mayo Clinic of giving as much as 2 or 3 drachms (from 7.4 to 11.1 cc.) of hydrochloric acid at a meal.

A Case for Diagnosis (Fox-Fordyce Disease?). Presented by DR. HOWARD EARLE TWINING.

J. W., a Negro aged 57, presents lichenified areas of the axillae and the scrotum. The more recent lesions are distinctly papular. The condition began about twelve or fifteen years ago with a small itching area in the suprapubic region. This has gradually spread until at present it involves the scrotum, the groins, the lower part of the abdomen, the lateral aspects of the chest and the axillae. Roentgenologic examination of the chest showed no abnormality. Application of an ointment containing 10 per cent juniper tar produced relief of itching but little change in the lesions.

DISCUSSION

DR. JOSEPH V. KLAUDER: The diagnosis is open to question. The involvement is too unusual for Fox-Fordyce disease.

DR. FRED D. WEIDMAN: Sometimes hyperkeratotic lesions appear on the skins of Negroes who do not maintain any notable degree of cleanliness. I am wondering whether in this patient the simple item of filth does not enter into the development of these lesions. The linear distribution on the sides of the chest suggests

creases in the skin in which dirt would accumulate and perhaps accentuate the hyperkeratosis against these dirtlike substances.

DR. JOHN H. STOKES: I was glad to hear Dr. Klauder qualify this diagnosis. I confess that to me the condition is not Fox-Fordyce disease. It is chronic lichenoid eczema in a Negro, possible with an element of vagabonds' disease.

DR. JOSEPH V. KLAUDER: This condition improved nicely with juniper tar. My associates and I have gradually increased the strength of the preparation and are now using it pure, painting it over the lesions. The patient tolerates it well.

A Case for Diagnosis (Psoriasis?). Presented by DR. DONALD M. PILLSBURY.

W. E., a white man aged 57, presents a hyperkeratotic, sharply demarcated, fissured dermatitis with a varying degree of erythema on the palms and the flexor surface of the left wrist. There is slight pitting of the finger nails. The condition had its onset in 1931 in a patchy, eczematoid dermatitis of the palms and wrists, which usually improved during the summer. Hyperkeratosis has increased. The general physical examination has shown no significant findings. Serologic tests of the blood were negative. Scrapings showed no fungi on direct examination or culture. A patch test with tracing paper which the patient uses in his work gave negative results.

DISCUSSION

DR. H. J. SMITH: I think this is a fungous infection.

DR. JOHN H. STOKES: I suggest that the old-fashioned plaster of 40 per cent salicylic acid be applied over this lesion and left on for two days and that the palm be peeled off and ointment of lead oleate applied. Another thing that might prove helpful is a year's persistent use of sulfur ointment U. S. P.

DR. JOSEPH V. KLAUDER: I believe the condition is ordinary eczema. I recommend painting it with undiluted juniper tar or coal tar. I suggest that an ointment of from 8 to 10 per cent juniper tar be used on the palmar lesion and that the strength of the preparation be gradually increased until it is used undiluted.

DR. FRANK V. KNOWLES: I think the condition is an occupational dermatitis. The patient is a draftsman, and the condition extends up the wrist. It is not symmetrical on both wrists but occurs on the palms with an extension up the wrist. I think if that man were instructed to place his hands in the position in which he works and the table he uses were inspected for areas of elevation and depression, this condition would be found to be a marginating outbreak at points of irritation.

NOTE.—Treatment by regular applications of a strong sulfur ointment (25 per cent), as suggested by Dr. Stokes, has produced considerable improvement.

FRANK C. KNOWLES, M.D., *Chairman*

Nov. 19, 1937

THOMAS BUTTERWORTH, M.D., *Secretary*

Pityriasis Rosea (Extensive Involvement). Presented by DR. ELMER R. GROSS, Wilmington, Del. (associate member).

N. J., a Negro aged 11 years, shows a widespread oval papulosquamous eruption on the extremities, the face, the scalp and the trunk. The lesions on the trunk are arranged with their long axes in the lines of cleavage. The herald patch is on the left forearm. The condition had its onset three weeks ago, with an isolated patch on the middle of the left forearm and gradually spread until it

became generalized. Medical examination showed no abnormality, except for posterior auricular, cervical, inguinal and epitrochlear lymphadenopathy.

DISCUSSION

DR. FRED D. WEIDMAN: My diagnosis is pityriasis rosea of the papular variety. The one thing that attracted my attention particularly was the tremendous amount of lymphadenopathy. One of the epitrochlear nodes is as large as any I have seen in a child under any circumstances. Has any other member seen a similar condition in pityriasis rosea?

DR. EDWARD F. CORSON: I think that in Negroes one is more likely to find papular lesions than flat plaques.

DR. J. P. GUEQUIERRE: I have noticed that pityriasis rosea is apt to be more extensive and severe in Negroes. I should like to hear from some of the more experienced men as to whether the clinical features of the disease are changing. In the last few years I have observed a number of cases in which the eruption has crept up the neck and even involved the scalp; and the primitive plaque, it seems to me, is no longer in the usual site. In one case it was on the dorsum of the right foot, a site at which I had never seen it.

DR. FRANK C. KNOWLES: I have noticed what Dr. Guequierre has just mentioned—that recently there has seemed to be a certain amount of involvement of the neck and even of the lower portion of the face in pityriasis rosea. The so-called mother spot or primitive plaque seems to be appearing in other locations than the lateral surface of the trunk.

Argyria. Lupus Erythematosus of the Scalp. Essential Shriveling of the Conjunctiva (Ocular Pemphigus), with Ocular, Oral and Vulvar Lesions. Presented by DR. JOSEPH V. KLAUDER.

M. G., a white woman aged 55, was presented at a meeting of this society on Nov. 11, 1932 (ARCH. DERMAT. & SYPH. **27**:718 [April] 1933). The diagnosis at that time was lupus erythematosus of the scalp, the conjunctiva and the buccal mucosa and argyria. The diagnosis of lupus erythematosus of the conjunctiva and the buccal mucosa, I believe now, was erroneous. The evolution of the conjunctival and oral lesions and the subsequent involvement of other mucous membranes justify the diagnosis of so-called pemphigus of the mucous membranes (ocular pemphigus and essential shriveling of the conjunctiva). A scaly eruption developed twenty-seven years ago on scattered areas of the scalp. After undergoing involution, the involved areas remained bald. Oral lesions first appeared in 1920 and have persisted. Small blisters appear from time to time on the buccal mucosa, the lips and the tongue. A 25 per cent solution of mild protein silver was applied twice daily for five years. Argyria appeared in 1929. About that time the patient noted a burning sensation and a mucoid discharge from her conjunctivae. In July 1937 lesions appeared on her vulva. The urinary stream is distorted, urine dribbling over the vulva. On the scalp there are extensive atrophic bald areas and scattered scaly erythematous lesions. The palpebral conjunctivae are dry and thickened, and at one area there is union of the palpebral and the bulbar conjunctiva. A solitary vesicle has been observed on the conjunctiva. On the buccal mucosa there are scattered rounded red areas. White patches and linear lesions on the inner surfaces of the lips, the tongue and the buccal mucosa resemble lichen planus as well as leukoplakia. Solitary vesicles have been observed on the buccal mucosa and the inner surfaces of the lips. The alveolar processes are considerably shunken and have almost disappeared. The teeth are absent. In some places there is union of the buccal mucosa with the mucosa covering the remains of the alveolar processes. The pharynx and the nasopharynx are normal. There are rounded areas of redness on the outer part of the nasal mucosa and on the mucosa of the anus. There is considerable shriveling of the vulva. The labia minora are united, and the entrance to the vagina is almost

obliterated. In the center of the area of union there is a dull red area similar to the oral lesions and surrounded by a narrow white zone. The urethra cannot be identified.

DISCUSSION

DR. FRANK C. KNOWLES: I think that many dermatologists are unfamiliar with what is spoken of by ophthalmologists as "ocular pemphigus." Recently at the Pennsylvania Hospital I was called in to see a white woman with vesicles and small blebs of the conjunctiva for whose condition the ophthalmologist had made the diagnosis of conjunctival pemphigus. There were no blisters on the cutaneous surface. The case was the second of that description that I had ever observed. The pemphigoid lesions are limited to the conjunctiva and are followed by shriveling.

Sarcoma in a Dog. Presented by DR. JOSEPH V. KLAUDER.

A female bulldog aged 9 years shows a "lump" which first appeared on the skin of the right side in February 1937 and gradually grew to about the size of half a dollar. In May 1937 it was excised. In the area of excision another "lump" formed, which in turn gradually enlarged. On the right flank there is an infiltrated hairless plaque which measures 5 by 3 cm. On its posterior part a circumscribed, rounded nodule can be palpated through the skin. The lesion is neither inflammatory nor pigmented. The overlying skin is intact, but the hair is absent. The regional lymph nodes are not palpable. A melanotic melanoma was diagnosed histologically.

Tuberculosis (Distinctive Type) in a Negress. Presented by DR. JOSEPH V. KLAUDER and DR. ELMER R. GROSS, Wilmington, Del. (associate member).

H. G., a Negress aged 37, was admitted to an ophthalmologic hospital on March 15, 1935, with a diagnosis of uveitis of both eyes. On admission vision of the right eye was 6/9 and of the left eye 6/15. The Wassermann reaction of the blood was strongly positive, but the reaction of the spinal fluid was negative in all phases. The patient received 50 injections of bismuth subsalicylate and 36 injections of neoarsphenamine between March 1935 and November 1937 and potassium iodide orally during the periods between injections. In November 1935 the Meinicke reaction was weakly positive, but in August 1936 the Wassermann and the Meinicke reaction were negative. The cutaneous involvement began one year ago, as a solitary lesion on the right thigh. This was followed by a number of discoid, elevated, infiltrated plaques, most numerous on the extremities but also involving the face and the back. The lesions have either scaly or smooth surfaces, and a few are atrophic and depressed. The latter characteristics are best noted on the scalp. The patient has lost 9 pounds (4 Kg.) in the past year. She is well developed but poorly nourished. The temperature is 99.4 F. Otherwise the physical examination showed no abnormality. Slit lamp examination revealed the typical picture of uveitis of probable tuberculous origin. Recent examination showed the vision of the right eye to be limited to perception of movements of the hand and that of the left eye 6/15. The tuberculin test with a dilution of 1:10,000 gave negative results. Histologic examination showed a typical tuberculous infiltrate, with associated giant cells and necrosis, characteristic of bacillary tuberculosis as it affects the viscera.

DISCUSSION

DR. FRED D. WEIDMAN: There are three certain respects in which tuberculosis in the American Negro differs from Boeck's sarcoid: 1. In the early stages the lesions are often psoriasiform and may be mistaken for psoriasis. 2. Not uncommonly they eventually ulcerate. 3. There is notable adenopathy. In Boeck's sarcoid, to be sure, there may be some adenopathy, but not the huge amount often met eventually in patients with this condition. These criteria are enough to differentiate this infection not only from Boeck's sarcoid but from Schaumann's

disease. Incidentally, Schaumann believes that his disease is not tuberculosis but a form of lymphoblastoma. He calls it benign lymphogranulomatosis. It is necessary, therefore, to differentiate Boeck's sarcoid, Schaumann's disease and this anergic form of tuberculosis in the American Negro. In the last condition the lungs become involved with tubercle bacilli, as in the original case reported by Dr. Klauder and me.

DR. JOSEPH V. KLAUDER: I think this case is typical of what Dr. Weidman and I first pointed out. There has been considerable controversy regarding the status of this type of infection. One writer does not believe it represents any particular features distinct from other forms of tuberculosis; others place it in the group of sarcoid. It seems to me inescapable, however, that it is a distinctive type of tuberculosis that is characteristic of the American Negro. To my knowledge, one does not see it except in the American Negro. (I do not know if Negroes in other parts of the world have this form of tuberculosis.) The clinical features are distinctive. There is a definite process of evolution—first the infiltrated sarcoid-like plaques, then the scaly psoriasiform type of lesions and finally atrophy with scar formation. Involvement of the scalp is characteristic. The enlarged lymph nodes and the negative tuberculin reaction and later the frank evidence of pulmonary tuberculosis complete the clinical picture. One writer recently found a resemblance to Schaumann's disease and osseous changes characteristic of Schaumann's disease. Nevertheless, though it is granted that there is a relation, I think one can regard this as a distinctive form of tuberculosis. To my knowledge, Schaumann's disease does not have all these features.

Dermatitis Venenata (Mercury and Its Salts). Presented by DR. ELMER R. GROSS, Wilmington, Del. (associate member).

N. A., a white women aged 23, was first seen in October 1937, when a wet dressing of mercurophen (sodium oxymercuryorthonitrophenolate) in a solution of 1:7,500 was applied to a pyogenic lesion on the hand. This solution caused an acute dermatitis confined to the area of its application. Patch tests were performed with 3 per cent ointment of mild mercurous chloride, 3 per cent ammoniated mercury, tincture of metaphen, mercurochrome, a 1:7,500 solution of mercurophen, 2 per cent yellow mercuric oxide ointment, 50 per cent solution of tincture of iodine U. S. P., tincture of merthiolate, a 1:10,000 solution of mercury bichloride and mercuric salicylate. All the tests, including one with adhesive plaster, produced pronounced erythema with vesicles, except those with mercurochrome, with tincture of merthiolate and with tincture of iodine, which gave negative results. The pigmentary remains of the positive reactions may be seen on the forearms. The positive reaction on the forearm was produced by 3 per cent ointment of mild mercurous chloride which the patient applied for this meeting.

DISCUSSION

DR. HERMAN BEERMAN: Has something happened to ammoniated mercury, or have patients become more sensitive to it? A few years ago I commonly used 10 per cent ammoniated mercury, and now I am afraid to give 2 per cent to most persons, lest they react unfavorably.

DR. JOSEPH V. KLAUDER: I have always had respect for ammoniated mercury. I think the official ointment should not be 10 per cent. As a routine I use ammoniated mercury in about 3 or 4 per cent strength. I find a combination of ammoniated mercury and salicylic acid is more likely to cause irritation than either preparation alone.

DR. REUBEN FRIEDMAN: I used a 3 per cent ointment of ammoniated mercury and had so many untoward results that I reduced its strength. Since then I have observed no reactions.

DR. THOMAS BUTTERWORTH, Reading, Pa.: The report of sensitiveness to mercurophen as well as to ammoniated mercury seems exceptional. I have a

number of patients who I thought were sensitive to ammoniated mercury and with whom I used mercurophen successfully. Recently I have been taking 1 grain (0.065 Gm.) of mercurophen, dissolving it in 10 cc. of warm water and stirring it into a proprietary ointment base in sufficient quantity to make an ounce. This makes a brilliant yellow cream which almost every patient will tolerate—even those who are sensitive to ammoniated mercury. Because of the base, it will take hold on a wet surface.

Lichen Planus in a Syphilitic Patient. Presented by DR. SIGMUND S. GREENBAUM and DR. SIMON KATZ.

R. M., a Negress aged 20, states that on Oct. 1, 1936, a papular eruption developed on the face, the scalp, the trunk and the extremities. There was no history of a primary lesion. A diagnosis of secondary syphilis was made. At present there is a dark, hyperkeratotic papular eruption over the face, the trunk and the extremities. Pelvic examination showed the floor of the vagina to be hard, infiltrated and ulcerated and the cervix chronically inflamed. Wassermann tests on Oct. 10 and Dec. 1, 1936, were strongly positive; on Feb. 9, 1937, the reaction was negative. A histologic section from the left arm showed a smooth surface covered by a moderate excess of hyperkeratotic substances; the epidermis was hyperplastic, the interpapillary pegs having the rather broad, more or less acuminate configuration seen in cases of lichen planus. Treatment consisted of eighteen injections of from 0.15 to 0.6 Gm. of neoarsphenamine between Dec. 1, 1936, and April 14, 1937, eight injections of bismuth subsalicylate between April 20 and June 8, 1937, and sixteen injections of from 0.3 to 0.6 Gm. of neoarsphenamine between June 29 and Oct. 12, 1937.

DISCUSSION

DR. FRED D. WEIDMAN: Histologically I have never seen a more typical picture of lichen planus. The surfaces of the lesions are shiny and blue-black, making one think more of the color of stove polish than of any other pigmentary material.

DR. JOSEPH V. KLAUDER: I think the picture is typical of lichen planus. The clinical features are consistent with the appearance of that disease in the Negro, particularly the psoriasiform character of the lesions. One may speculate as to the relation of the eruption to the neoarsphenamine therapy. A type of arsphenamine dermatitis lichen planus has been described. Jonathan Hutchinson first described the occurrence of zoster after the administration of arsphenamine and pointed out that arsenic had been used in the treatment of zoster. He said that he would call the attention of his homeopathic friends to that fact. Consistent with that, lichen planus may follow the administration of arsenic—at least, it has in this case.

DR. FRANK C. KNOWLES: I cannot help thinking that the drugs have had something to do with the curious appearance of these lesions. Bismuth subsalicylate may have been a factor in the production of the curious slate-blue color of some of the lesions, and the keratotic elements point distinctly toward an arsenical origin.

DR. FRED D. WEIDMAN: Some of the lesions are definitely verrucous.

DR. DONALD M. PILLSBURY: There are a number of reports in the literature of typical lichen planus following arsphenamine therapy, and this fact has caused some ridicule by the Germans of the French method of treating lichen planus with arsphenamine.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: Is it not unusual to have true lichen planus of the face?

DR. JOSEPH V. KLAUDER: Yes, it is. The lesions occur on the eyelids in this patient, which I think is most extraordinary.

DR. SIGMUND S. GREENBAUM: Was not the diagnosis of lichen planus entirely or largely based on the histologic observations? Was there not considerable fibrosis in the lesions? Some of those lesions feel unusually firm.

DR. FRED D. WEIDMAN: The cellular infiltration in the pars papillaris was remarkably dense and sharply demarcated from the deeper parts of the corium.

Erysipelas Carcinomatosum. Presented by DR. JOSEPH V. KLAUDER.

J. M., a white woman aged 63, had most of her left breast removed for carcinoma in January 1934. An operation was performed on the same breast in December 1936. Between the time of the latter operation and March 1937 about ten roentgen treatments were given to the remains of the left breast. In August 1937 the skin over the left side of the chest became red, and an oozing area appeared in the center of this redness. In June 1937 the skin over the right breast became reddened. The general condition of the patient has been good. In the center of the left side of the chest there is a bright red oozing area approximately the size of one's palm, which resembles Paget's disease. Surrounding this on all sides the skin is moderately red. This zone of erythema is infiltrated and has irregular borders. Palpation shows scattered pea-sized lesions in the skin. The surface of the involved areas is intact; there is no dermatitis. The right breast is considerably infiltrated and hard, and the nipple is retracted. The skin of the breast and the adjacent region is reddened, and the borders are irregular. The skin is more infiltrated than that on the left side. There is some thickening suggestive of beginning cancer *en cuirasse*.

DISCUSSION

DR. FRED D. WEIDMAN: Did only one side of the chest receive irradiation?

DR. JOSEPH V. KLAUDER: The left side only.

DR. SIGMUND S. GREENBAUM: Objectively, there are three conditions: One is nodular; one is the fairly wide erosive area in the center, and one is this diffuse, noninfiltrated superficial erythematous flush beyond that. Of course, in cases of malignant growth secondary infection is common, particularly if the parts have been opened spontaneously or by treatment. It would be difficult to believe, unless histologic examination definitely shows it, that this diffuse flush represents malignant lymphangitis, without palpable evidence of such a state.

DR. JOSEPH V. KLAUDER: In that central red area I should subscribe to the possibility of radiodermatitis. The condition looks like healing, perhaps granulating, tissue, but I do not think that radiodermatitis is sufficient to explain all the lesion.

DR. FRED D. WEIDMAN: One of the sections from the left side shows definite carcinoma of the prickle cell type. It was removed from the central infiltrated portion. The section from the margin of the reddened area on the left side does not show carcinoma. It also came from an infiltrated portion. I think, though, that when I cut deeper into the block I may get the picture of carcinoma. (NOTE.—This turned out to be true.) It is singular that the right side did not receive any irradiation and yet shows cancer. The latter is not a simple extension from the cancer of the breast; it is clearly progressing from the epidermis and is difficult to explain. I wonder if the erythematous flush is not referable to the products of the cancer diffusing through the lymphatic vessels; in the erythematous parts seen tonight, in which one cannot palpate any infiltration, the color completely disappears on diascopic pressure. The section from the left side shows blue, mucinoid material in the lymphatic vessels, which might indicate the abnormal substance which is provoking the red color yet farther out. I think the term "erysipelas" is not well chosen. The condition is an erysipelatous erythema, perhaps, but I strongly doubt that the part farthest out will be shown to contain cancer cells; one cannot feel any infiltration, and one can express all the red color with the diascope.

DR. JOSEPH V. KLAUDER: That may be so, but I think that if this block is studied further or if more sections are made the histologic picture which has been described for this condition will show that the diagnosis is justified.

CHICAGO DERMATOLOGICAL SOCIETY

OTTO H. FOERSTER, M.D., *President*

Oct. 20, 1937

H. RATTNER, M.D., *Secretary*

Argyria from Local Application of Mild Protein Silver. Presented by DR. OLIVER S. ORMSBY.

A. S., a woman aged 39, noted a slight discoloration in the nasolabial folds of the face nine months ago. She states that the discoloration varied from time to time but never disappeared. A silver salt was applied in the nose for three years. This was discontinued two months ago. In addition to this, a dye containing silver has been used on the hair for the past twelve years.

Examination shows a slate blue discoloration of the skin of the entire face, more evident about the nasolabial folds. Because of the complexion of the patient it is difficult to be certain whether other exposed areas are becoming involved.

Solid Edema of the Face. Presented by DR. OLIVER S. ORMSBY.

M. B., a man aged 39, presents a cutaneous disease which began approximately eleven months ago. There have been repeated attacks of acute inflammation, lasting a week or more and followed by short periods of quiescence before renewal of the inflammation. The patient described the first attack as involving the entire nose, the forehead and both cheeks, beginning with redness over the bridge of the nose. Some swelling and edema and probably a slight increase in color remained between acute attacks. Superficial pustulation is said to have occurred during some of the attacks.

When the patient was first examined during an attack, in the aforementioned areas the skin was bluish red and swollen, the eyes being almost closed because of edema of the lids. He complained of pruritus. For four months treatment consisted of injections of nonspecific protein administration of vaccines and of dextrose and roentgen therapy. These measures produced no appreciable effect.

Sulfanilamide therapy was started and continued for ten days before a severe reaction to the drug occurred. This included elevation of temperature to 103 F., severe headache and a generalized maculopapular and erythematous eruption. The face was swollen and deep purplish red. The entire reaction cleared in about five days. The local condition of the face has not recurred for two months.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: The livid appearance of the face, with edema and telangiectasia, suggests polycythaemia vera or lymphatic leukemia. However, in view of the absence of abnormal findings generally and on account of the history, I agree with the diagnosis of lymphedema, probably on a basis of subacute recurrent lymphangitis. The search for etiologic factors in this condition is often fruitless, and for that reason I am pleased to learn of the response to sulfanilamide therapy, in spite of the fact that there was a serious systemic reaction to the drug.

DR. RICHARD S. WEISS, St. Louis: I have observed a number of somewhat similar cases and have found that if the sulfanilamide therapy is not kept up for several weeks after the acute symptoms have subsided, the disease will recur.

DR. MARCUS R. CARO: In a case I observed last week a patient had been given a total of 100 grains (6.48 Gm.) of sulfanilamide over a period of six days for the treatment of postoperative fever. Diarrhea and vomiting developed and then a toxic erythema appeared. Several days later agranulocytosis developed, and in spite of repeated blood transfusions and the use of pentnucleotide, the patient died.

A **Case for Diagnosis (Poikilodermatomyositis Dermatomyositis of the Type of Poikiloderma Congenitale?).** Presented by DR. CLARK W. FINNERUD and DR. H. N. SANFORD (by invitation).

W. O'T., a boy aged 5 years, was first seen July 23, 1937, because of a generalized cutaneous eruption which had been progressing from early infancy. The family history was normal, aside from the fact that his mother suffered from migraine and asthma throughout pregnancy. The patient's weight at birth was 7 pounds (3.2 Kg.); delivery was normal, and he progressed normally with artificial feeding until he was 2 weeks old. At this time a generalized reddish apparently macular cutaneous eruption developed, and he became irritable, which he evidenced by crying as if in pain when he was picked up. This continued until he was 4 months old, when it was noticed that he kept his legs continuously flexed and would cry when they were straightened. He held his head up at 3 months, sat at 7 months and crawled at 18 months. He had his first tooth at 17 months. He began to walk at 2 years and walked for a few weeks at that time but only for short intervals since, being bedridden almost continuously.

The cutaneous eruption has persisted, with exacerbations. The mother states that when the eruption is better she is apprehensive, because his temperature rises and he has more pain in his limbs. The boy has had frequent attacks of tonsillitis but has had fewer infections of the throat since tonsillectomy two years ago. He has had measles, chickenpox and pneumonia, the last of which seriously threatened his life. He has been repeatedly hospitalized in various sections of the country, but a definite diagnosis apparently has not been made.

He is unable to extend his legs; yet all his reflexes are normal. Active or passive motion of his joints elicits exquisite tenderness. He is apprehensive and speaks rather indistinctly. He holds his head down, probably because of pain in the neck and he gives the impression of apathy. Pediatricians do not consider him subnormal mentally. His temperature is practically continually between 100 and 104 F., usually rising late in the afternoon. On a few occasions he has had no elevation of temperature for a few days at a time. The liver and the spleen are palpable.

The muscles of the extremities are atrophic, and the skin and the underlying tissues feel sclerodermatous in these areas. The face is red and shows a pinkish to bluish red maculonodular, slightly indurated eruption which in places resembles lupus pernio. A similar maculopapular and maculonodular eruption is present on the neck and the upper extremities, especially on the extensor surfaces.

Histologic examination showed nonspecific mild inflammatory changes, apparently compatible with the cutaneous changes of poikilodermatomyositis. The epidermis and the corium were slightly thinned. There was rather marked dilatation of the blood and the lymph vessels throughout the corium, associated with slight edema and mild lymphocytic infiltration, chiefly of the lower part of the corium. There was a distinct increase of fibroblasts in the lower part of the corium and the hypoderm. The biopsy specimen was not taken deeply enough to include muscle.

Examination of the blood showed low grade anemia, 3,500,000 erythrocytes and 5,000 leukocytes. The differential count was normal (no eosinophilia). The Wassermann and the Kahn reaction were negative. Chemical analysis of the blood showed no abnormality, except that the calcium content, 9.5 mg. per hundred cubic centimeters, and the amount of vitamin C, 0.58 mg., were low normal; the sedimentation time was markedly increased. The urine was normal except for markedly increased creatinine (73.2 mg. in a twenty-four hour specimen). A culture of blood showed no abnormality, and there was a negative reaction to an intracutaneous tuberculin test with 1:1,000 dilution. There was no agglutination with the organism of typhoid, of paratyphoid or of Malta fever, with Brucella or with Proteus A or B. Roentgenograms showed the skeleton to be normal.

Against the theory that this condition is a streptococcic infection, as Still's disease is often presumed to be, may be mentioned a negative response to sulfanilamide.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: The term poikiloderma is being used more and more to describe end-stages in the skin of various types of such serious diseases as dermatomyositis, lupus erythematosus and the lymphoblastomas. In this child the features which suggested dermatomyositis were the doughy consistency of the muscles of the forearms and the calves and the atrophy of the muscles of the shoulder girdle. The creatininuria is of interest. The outlook for the future of this child is not good, in spite of the fact that the condition has proceeded slowly over the past four or five years.

DR. OTTO H. FOERSTER, Milwaukee: I think this condition is dermatomyositis. In several cases which I have observed adults have presented much the same picture. I think some importance can be attached to the creatininuria as evidence of muscular injury and as a helpful point in diagnosis.

DR. CLARK W. FINNERUD: Under the title "Still's disease" pediatricians recognize a chronic arthritis occurring in infants and children under 5 years of age and associated with general lymphadenopathy, including splenomegaly, an erythematous eruption similar to the one present in this patient and anemia. When I first saw this patient, six weeks ago, my impression from the eruption alone was that the condition might be an unusual form of leukaemia cutis, in spite of its long duration and the age of the patient. An unusual form of lupus erythematosus was also considered. Thomson described a group of cases of poikiloderma congenitale (*Brit. J. Dermat.* **48**:221 [May] 1936) in which the cutaneous changes were practically identical with those seen in this patient, but there were no associated changes in the muscles. Poikiloderma and dermatomyositis occurring together have been shown by Dowling (*St. Thomas' Hosp. Rep.* **1**:150, 1936) and others to merge into one another and to manifest the different features in greatly varying degrees. Petges apparently coined the term poikilodermatomyositis, but no case has been found in the literature in which the combination of symptoms began in a patient so young as the present one. This patient presents several apparently unique features, and it may well be disputed whether it is proper to consider the dermatomyositis as of the poikiloderma congenitale type, because of the papular element in the lesions during periods of activity and because of the small amount of telangiectasia.

Scleredema Adultorum. Presented by DR. E. A. OLIVER.

J. A., a carpenter aged 46, states that his present condition began on Aug. 15, 1937. When he was seen in September, it had spread rapidly to involve the entire upper portion of the body. He has been ill several times in recent years. In 1929 he had pneumonia. In August 1936 he was examined at the Veterans Administration Facility, Muskogee, Okla., and told he had pernicious anemia. Up to the time of his entrance into the Veterans Administration Facility at Hines, Ill., he had been taking treatment for this condition. He is inclined to consider the medication prescribed for his anemia as the cause of the cutaneous condition. The skin of the face, the neck, the arms, the chest, the abdomen and the back is smooth and hard and cannot be picked up between the fingers. There is solid edema, and the skin does not pit on pressure. The face was so badly involved three weeks ago that his eyes were opened with difficulty. The face is masklike. There is interference with normal action of the muscles and the joints.

The basal metabolic rate on five determinations was +1.2, —2.6, +3.9, —6.5 and —11.7 per cent. Examination of the blood on September 15 showed 4,340,000 erythrocytes, 770 leukocytes and 80 per cent hemoglobin. Urinalysis showed no abnormality. The Wassermann reaction was negative. Roentgenograms of the heart, the lungs, the gastrointestinal tract and the gallbladder were normal. Dextrose tolerance tests showed no abnormality; the chloride content of the blood was 505, the sugar content 105.2, the calcium content 10.4 and the inorganic phosphate content 2.9 mg. per hundred cubic centimeters.

Scleroderma (Localized). Presented by DR. WILLIAM A. ROSENBERG (by invitation).

L. U., a woman aged 19, states that about five years ago she noticed a bluish discoloration on the anterior surface of the thigh, which spread upward toward the hip and later became pigmented. About a year later she noticed a hardening in the center of this pigmentation. The hardening gradually enlarged. She frequently complained of chilly sensations and tired easily.

Chemical analysis of the blood showed 9.1 mg. of calcium, 32 mg. of protein nitrogen, 95 mg. of sugar and 5 mg. of phosphorus per cubic centimeter. The basal metabolic rate was +5 per cent. The Kahn test gave a negative result.

DISCUSSION ON PAPERS OF DR. OLIVER AND DR. ROSENBERG

DR. H. E. MICHELSON, Minneapolis: I agree with the diagnosis as presented, and I think the patient shows all the features of that condition. The two patients with this condition that I have seen before were in their teens, and this is the first time that I have seen such a condition in a person of mature years. One must consider the acute stage of scleroderma, but the rapid recession rules that out fairly well.

DR. S. W. BECKER: I agree with the diagnoses in both cases.

DR. M. H. EBERT: I inquired whether the man in the first case had a sore throat or an acute infection preceding the appearance of the scleredema. I was told that he did have a sore throat. This is frequently true in scleredema of Buschke.

DR. THEODORE CORNBLEET: I think the first case is one of scleredema adultorum. In my experience with scleroderma, if the hands are involved, they are the last areas to return to normal. In this case the hands were the first to improve. In the second case I think the lesions are those of morphea, limited to the thighs and showing a distribution following a nerve.

DR. E. A. OLIVER: I am glad to hear the members agree with the diagnosis. My case is the first that I have observed which I felt must be one of scleredema. The fact that the onset was accompanied by sore throat and difficulty in swallowing and the rapid improvement in the condition serve to substantiate that diagnosis.

DR. THEODORE CORNBLEET: The rationale, perhaps, for the use of ammonium chloride is its production of acidosis. Since calcium is more soluble in an acid medium, it has been demonstrated that there is an increase of calcium in the skin in scleroderma. The relative acidity induced by the ammonium chloride might cause some decrease in this calcium deposit.

DR. WILLIAM A. ROSENBERG (by invitation): Ammonium chloride was tried in this case, with no result. As Dr. Schmidt suggested treatment with a pancreatic preparation, I wonder if he would tell us more about it.

DR. FREDERICK R. SCHMIDT: In a few cases I have used whole pancreas by mouth and pancreatic ferment by subcutaneous injection. I observed favorable results in two cases of localized scleroderma.

A Case for Diagnosis. Presented by DR. E. A. OLIVER.

F. S., a man aged 44, born in Czechoslovakia, a machinist, is presented through the courtesy of Dr. Frank Theis.

The patient has suffered from Buerger's disease since November 1936. He complains of coldness of both feet and legs, a bluish discoloration (dependent rubor) and continuous rest pains for about one month prior to hospitalization. On July 7, 1937, he entered the Presbyterian Hospital, complaining of pain and coldness in the legs. Pulsations were not palpable in the anterior tibial, the posterior tibial or the popliteal artery of either leg. The oscillometer index was 0 on the lower part of the left leg and ankle and almost 0 on the lower part of the right leg and ankle.

Within three weeks the patient was completely relieved and was discharged. He continued treatments two or three times weekly throughout August and September.

On Sept. 18, 1937, his right leg was in excellent condition. The inside midportion of the left calf was swollen, indurated, sensitive and painful. The pulse rate was 80 and the temperature 98 F. There was no fever at any time.

The center of the area contains a scar from an ulcerated lesion the patient had during the war.

From the initial area, which subsided a little, a posterior area became involved; small, almost imperceptible bluish areas appeared. These gradually approached the surface and became necrotic, and five walnut-sized black superficial necrotic areas appeared. Patent superficial veins extend directly through these areas and are not thrombosed. There is apparently no occlusion of the veins. The entire course has been afebrile, and there are excruciating pain and tenderness in the affected area. The erythrocyte count was 9,000. The urinalysis showed no abnormality.

DISCUSSION

DR. E. A. OLIVER: I have nothing to add, except that the man has had Buerger's disease and that the cellulitis has subsequently developed in the lower part of the left leg. Dr. Brunsting has suggested that the cellulitis is probably streptococcic and that the patient should be given sulfanilamide therapy. I am going to suggest this to the surgeon who is caring for him.

A Case for Diagnosis. Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

J. L., a white boy aged 10 years, was admitted to the Bobs Roberts Memorial Hospital for Children on July 30, 1937, with a generalized maculopapular erythematous eruption which has varied from day to day for four monhs, daily elevation of temperature at times up to 105 F. for six weeks, intermittent sore throat for six weeks, loss of weight for four weeks, occasional pains in the joints and the muscles for six weeks and brownish erythematous plaques, with a few papules near the border on the back and the neck for two weeks.

He was in good health until six weeks before admission, except for the generalized eruption, which had caused no symptoms and had not kept him from school. At that time he began to have pains in the joints and the muscles and was found to have a daily elevation of temperature. Prior to admission a diagnosis of acute rheumatic fever and streptococcic sore throat was made, and one physician is supposed to have found malarial parasites in the blood. He had received sulfanilamide for six days and then quinine for eleven days shortly before admission. The eruption on the back and the neck appeared about two weeks before admission (three months ago) and has persisted. It is rather pruritic.

Examination at the time of admission showed an inconstant soft systolic murmur over the apex of the lungs. The joints of the right hand were swollen and tender. The right knee and both ankles were tender when passive motion was effected. There was mild generalized lymphadenopathy.

Examination of the blood showed 17,100 erythrocytes, 3,510,000 leukocytes and 62 per cent hemoglobin. The differential count showed 75 per cent polymorphonuclear neutrophils, 12 per cent lymphocytes, 4 per cent monocytes and 9 per cent eosinophils. No plasmodia were found. The Wassermann reaction was negative. A tuberculin test gave a negative result. The urine was normal. A roentgenogram of the chest showed the lungs to be clear and the heart of normal size. An electrocardiogram showed myocardial damage. Scratch tests revealed moderate reactions to milk, tomato, strawberry and egg white. Scrapings from the lesion showed no fungi.

While in the hospital the patient has received two 150 cc. blood transfusions. His general physical condition has improved, but the generalized eruption con-

times to appear and fade daily, and the eruption on his back and neck, while not as dark as at the time of admission, is of the same extent and continues to be somewhat pruritic.

Intracutaneous injection of a 1 per cent of solution of congo red into one of the papules near the border of the lesion on the back was followed by no retention of the dye.

Histologic examination of a lesion on the back showed the stratum corneum to be thickened and to contain many cells showing individual keratinization, many of which had basophilic nuclei. The stratum granulosum was thickened in some places and thin in others. Where it was thin some cells showed individual keratinization, extending upward from just above the basal layer. The stratum mucosum was thickened, with slight intercellular edema. Mitotic figures were especially abundant. In certain regions cells showing individual keratinization were seen in various levels. In the papillae and the superficial layers of the dermis there was a moderate perivascular infiltrate of round cells.

DISCUSSION

Dr. S. W. Becker: This boy is presented for diagnosis of the brownish plaques on the upper part of the chest and the back. Those who examined the microscopic section agree that there is a certain amount of keratinization of individual cells in the lesion, but on the basis of that a definite diagnosis cannot be made, and I should be glad to have some suggestions. The question as to whether the condition is associated with or independent of the rheumatic fever arises.

Dr. Richard S. Weiss, St. Louis: I cannot make any suggestion as to the patches, but I think the toxic erythema associated with rheumatic endocarditis places that particular eruption in the original erythema group of Osler.

Purpura Annularis Telangiectodes. Presented by Dr. M. H. Ebert.

A. O., a man aged 41, of English and Irish descent, first noticed red spots on the lower parts of the legs about two and a half years ago. These increased gradually in number and spread up the leg. About one year later little scaly crusts began to form near the ankle and to separate. In the last few months lesions have been appearing on the lower parts of the thighs. The patient has chronic prostatitis.

The lesions extend from the toes up the dorsum and the sides of each foot as far as the lower third of the thigh. Older lesions show the following picture: On the legs there is a brownish retiform discoloration which does not disappear when diascopic pressure is applied. There are bright red cayenne pepper puncta, most marked on the lower parts of the legs. These do not disappear under pressure. There are pinhead-sized dull red points which become paler when compressed. There are annular areas of atrophy, ranging in size from that of a match head to that of a split pea. Many of these have bright red points and dilated vessels at the border. The dilated vessels disappear when compressed, but the bright red points remain. The lesions which the patient describes as being most recent are on the midthigh and consist of pinkish macules the size of a match head, which do not entirely disappear under pressure. There are fine dilated vessels on the surface of these macules and an occasional fine bright red punctum that does not disappear when pressure is applied.

The reaction to Peck's moccasin venom test for capillary fragility was strongly positive on the lower part of the thigh and negative on the forearm.

The Wassermann reaction of the blood serum was negative.

Histologic examination of an early lesion from the thigh showed the epidermis to be normal. The principal changes were in the small vessels of the papillary and the subpapillary layer. Some of these were dilated and engorged with red cells, and in others the endothelium was swollen; in a few instances there was karyorrhexis of the endothelial nuclei, with diapedesis of the red cells. In others

there was considerable free hemorrhage in the connective tissue about the vessel, with a small amount of round cell infiltrate. Staining with prussian blue showed a trace of iron pigment.

Histologic examination of an old lesion from the leg showed more striking degenerative changes in the walls of the small vessels of the subpapillary zone than did that of the early lesion. In some there was pyknosis and karyorrhexis of the endothelial nuclei, associated with marked round cell infiltration of the walls of the vessels and the area about them. In some of these small vessels there was definite thrombus formation. Considerable hemorrhage appeared to have taken place into the corium, and some of the red cells had degenerated and formed pigment. In the deeper part of the corium this pigment had been phagocytosed by the reticular cells about the vessels. There were fragmentation and degeneration of the elastica about the areas of hemorrhage. The reaction to the prussian blue test for iron pigment was strongly positive.

DISCUSSION

DR. M. H. EBERT: The reaction to Peck's venom test for capillary fragility is interesting. It was negative in the skin of the forearm and positive in the area where the new lesions were. The diagnosis was based on the purpuric hemorrhages, the annular arrangement and the scar formation. To me the most interesting feature is the early lesions on the thigh. These are small groups of dilated vessels. In an occasional one I found a small punctate hemorrhage. The histologic picture was typical of Majocchi's disease.

DR. H. E. MICHELSON, Minneapolis: It might be interesting to have pictures of this condition taken under infra-red illumination. Some light might be thrown on the origin of the disease in that manner.

Chronic Lymphatic Leukemia (Nodular Ulcerative Type). Presented by DR. HARRY M. HEDGE.

H. M., a white man aged 51, presented himself at the outpatient department of the Evanston Hospital on June 14, 1937. The clinical picture resembled tularemia or sporotrichosis more than a cutaneous manifestation of leukemia. On the right little finger there was a small ulcer with undermined edges, and there was a line of nodular ulcerating lesions on the lymphatic vessels of the right arm. The patient had been cutting grass and weeds for the past five months and thought he had become infected from a cut while so employed. On several previous occasions small erythematous lesions appeared on the skin and were accompanied with considerable pruritus. There was an enlarged gland under the right axilla, but this was not painful and when aspirated yielded no pus. Considerable improvement of the ulcers has resulted from sponging with mercury bichloride and later from applications of cupric sulfate and internal administration of potassium iodide. Within the last months several ulcerated nodules have appeared on the scalp, the legs and the body. Cultures made from the pus and crusts showed no fungi and there was no agglutination with Bacillus tularensis.

Examination of the blood showed 5,200,000 erythrocytes, 96,000 leukocytes, 97 per cent of which were lymphocytes, and 87.6 per cent hemoglobin. The Wassermann and the Kahn reaction were negative.

Histologic examination showed the pertinent primary changes in the cutis, where there were irregular nodular perivascular infiltrations of mononuclear lymphocytes. Subcellular infiltrations were seen about the base of the hair follicles. These accumulations, which were found deep in the cutis, showed some fragmentation and degeneration of the cellular infiltrations. Above these areas the skin, although intact, showed slight acanthosis of the epidermis and moderate hyperkeratosis. One of the infiltrating type of cells was a large nongranular mononuclear cell with a definite basophilic cytoplasm and a round, densely hyperchromatic nucleus. An occasional cell resembling a megakaryocyte was seen.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: A patient presented from my clinic by Dr. Lynch had reticulo-endotheliosis, and the lesions looked surprisingly like those in this case.

DR. HARRY M. HEDGE: The interesting thing is that the condition resembled tularemia so much, with an ulcer on the little finger. The patient had been working in grass where there were wild rabbits. The tests were negative for that disease, however, and for everything else except leukemia. There were no lesions of the mucous membranes and never had been. Improvement under the medication given was limited to the local lesions.

Lupus Erythematosis Disseminatus. Presented by DR. THEODORE CORNBLEET and DR. EARL R. PACE (by invitation).

G. P., a white woman aged 30, states that four years ago she was sunburned. When the inflammation subsided, a red spot appeared on the nose. After several weeks a physician told her she had ringworm. Another said the condition was ivy poisoning. She used various forms of medication but got no relief. The lesions spread on the face and appeared on the hands, the arms and the legs. She has been treated with sulfanilamide, 10 grains (0.65 Gm.) four times a day, since Oct. 13, 1937. So far there has been no improvement in the condition of her skin.

Acute Lupus Erythematosus Disseminatus with Sensory and Motor Changes. Presented by DR. THEODORE CORNBLEET and DR. E. ROBBINS (by invitation).

A. S., a white woman 49 years old, has had an eruption on her face, neck, hands and knees for six weeks. In addition, there is marked difficulty in swallowing.

She became ill seven weeks ago with a cold and has since felt greatly fatigued. At the same time it became almost impossible for her to swallow solid food. She consulted an otolaryngologist but obtained no relief for her dysphagia. One week later an eruption appeared on the right upper eyelid; it spread to involve the face, the neck and the upper part of the chest. There was swelling of the face.

She had "sinus symptoms" after an attack of influenza and had an operation on her nose sixteen years ago. She believes her hearing is becoming progressively impaired. Several months ago she was burned by nitric acid.

Her face now shows a deep congestive erythema, with marked edema. The neck and the upper part of the chest are similarly involved, except for the edema. There is a scaling erythema over the backs of the fingers.

An otolaryngologist reported that her ear drums were retracted and that there was no discharge from them. He found the soft palate scarred as after tonsillectomy. The right side of the soft palate was paralyzed, and the uvula was drawn to the left. In the pharynx there was considerable frothy mucus in the pyriform sinuses, suggesting obstruction high in the esophagus. The vocal cords moved freely. There were no intrinsic lesions of the larynx. The consultant thought there was a suggestion of paralysis of the constrictor muscles of the pharynx and that the accumulation of mucus in the pyriform sinus was added evidence of this. He suggested fluoroscopic examination to observe the swallowing function and to rule out a high obstructive lesion of the esophagus.

Fluoroscopic examination of the esophagus and of the stomach showed no impairment of them, but no report was made of any observations on the pharynx.

The leukocyte count was 6,600, and the differential count showed 80 per cent polymorphonuclears, 16 per cent lymphocytes, 2 per cent mononuclears and 2 per cent eosinophils. There was 80 per cent hemoglobin. The Wassermann test of the blood was negative.

Histologic examination of a lesion on the chest showed atrophy of the epidermis and slight hyperkeratosis. The rete pegs were flattened. The papillary and the reticular layer of the cutis were composed of dense collagen fibers.

The neurologists have not had an opportunity to examine the patient.

Lupus Erythematosus Disseminatus Subacutus in a Child. Presented by Dr. M. H. Ebert and Dr. A. Slepyan (by invitation).

L. B., a Negress aged 11 years, presents an eruption which began about a year ago on the forehead. In the past four months a number of new lesions have appeared, principally on the face, the chest, the arms and the palms.

The mother states that the child seems to sleep a good deal. There is no cough, and the appetite is poor.

The parents, one sister and two brothers are living and well. Two children died at birth. The patient has had the usual diseases of childhood.

On the face are several plaques, varying in size from that of a match head to that of a finger nail and with slightly raised bright red borders. In the larger areas the center is depressed and scaly. Some are hyperpigmented and atrophic. There are a few in the scalp. In one large lesion on the forehead the follicular openings are exaggerated in the atrophic center. Both ears are markedly involved. In the right ear there seems to be crust formation. On the chest similar round plaques coalesce to form larger areas with a circinate outline. There is hyperpigmentation beyond the border. The lesions on the arms and the legs are about the same size and the infiltration is marked. There are multiple dull red flat papules varying in size from that of a match head to that of a split pea on the palms and the flexor surfaces of the fingers. Some of these are definitely depressed in the center. On the dorsa of the fingers the lesions resemble the ones on the arms. There are a few scaly relics on the lower part of the abdomen. The epitrochlear glands are moderately enlarged, and there is a hazelnut sized gland in the right axilla. There are a few shotty glands in the inguinal and the cervical region. There is nothing abnormal in the mouth. A roentgenogram of the chest showed a bilateral increase of the hilar markings extending into the pulmonary parenchyma. The Wassermann reaction was negative. Low grade fever is present.

Histologic examination showed the epidermis to be hyperkeratotic, markedly edematous and in places thinned to two layers of cells by colliquative necrosis of the basal layer. There were intense edema and vascular dilatation, associated with round cell infiltration of the upper third of the corium. There was some hemorrhage into the tissue. In the middle part of the corium the infiltrate was perivascular.

DISCUSSION ON LUPUS ERYTHEMATOSUS DISSEMINATUS

Dr. V. C. Belisario, Sydney, New South Wales (by invitation): Of these three cases the only one about which I have anything to say is the one in which the condition is acute. Concerning that I should like to ask whether the diagnosis of dermatomyositis might not be considered, from the appearance of the face and in particular of the fingers, where the redness is seen mostly around the nails and over the joints.

I have observed several cases of dermatomyositis with muscular stiffness like that in this case, and in all of these the distribution of the involvement of the fingers has been like that in the case presented today.

Dr. Richard S. Weiss, St. Louis: It is rather extraordinary to observe three such cases at one time. One of the things my associates and I have been working on recently in relation to this disease is careful roentgen study of the heart, with relation to the discovery of pericarditis. In the last case we observed, autopsy showed severe purulent pericarditis, with profound toxemia involving the kidneys and evidence of capillary changes through most of the tissues of the body. Another point is to try to demonstrate changes in the joints roentgenographically. We have not had the opportunity of opening any of the joints at autopsy, and perhaps by roentgen study it can be determined when the joints are involved. It appears to us that studies should be made from the standpoint of profound toxemia of bacterial or virus origin.

Dr. Oliver S. Ormsby: Dr. Cornbleet and I saw a patient who exhibited muscular involvement of the throat like that in the case he presented today.

These are the only two cases of disseminated lupus erythematosus in which I have seen that symptom.

DR. H. E. MICHELSON, Minneapolis: In spite of all the newer thoughts concerning disseminated lupus erythematosus, one must not forget that the condition can be produced by tuberculosis. Recently I had a patient whose eruption responded well to oral administration of sulfanilamide. The patient committed suicide, and autopsy showed him to have miliary tuberculosis.

DR. RICHARD S. WEISS, St. Louis: This patient might have an infection somewhere else that might have caused the eruption.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: At the meeting today there has been brought forward a wealth of material in which there is dermatologic evidence of serious underlying disease, and these three cases of disseminated lupus erythematosus are good examples. In one instance the process appears to be much more acute than in the others, and the prognosis should be decidedly guarded.

DR. M. H. EBERT: There were generalized fibrotic changes in the pulmonary field and cutaneous manifestations.

DR. THEODORE CORNBLEET: I appreciate Dr. Belisario's suggestion that dermatomyositis is the diagnosis in my case. I do not, however, feel that that is the correct diagnosis. This woman has been rather neurotic and hard to manage. She complains on manipulation and does not care to be manipulated in any way, and I think her complaints were misinterpreted as pain. My impression is that she has had disseminated lupus erythematosus from the beginning.

Idiopathic Hemorrhagic Sarcoma of Kaposi. Presented by DR. E. A. OLIVER and DR. RALPH H. SCULL (by invitation).

M. S., a Russian Jew, aged 60, complains of a lesion on the right foot that began three years ago on the dorsum of the second toe as a pea-sized blister containing watery fluid, which later changed to a serosanguineous discharge. The lesion gradually spread to the dorsal surface of the foot as a bluish-red-brown plaque. There is occasional pruritus.

Examination shows a bluish red raised plaquelike lesion involving the dorsum of the first three digits and the foot and sharply demarcated from the surrounding skin. The portion of the lesion involving the toes is soft and compressible, while that of the foot is firm. Over the outer surface of the heel there are some pigmented scars.

The Wassermann reaction was negative. Roentgenograms of the digits and urinalysis showed no abnormality. Examination of the blood showed 95 per cent hemoglobin, 62 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 30 per cent lymphocytes and 5 per cent monocytes.

Histologic examination of tissue from the dorsum of the foot showed some hypertrophy of the horny layer. In the cutis and the subcutis there were marked dilatation and new formation of blood vessels. A section stained with prussian (berlin) blue showed hemosiderin.

DISCUSSION

DR. DAVID LIEBERTHAL: The lesions on the heel are apparently not of long duration. They are, however, typical of Kaposi's sarcoma, as are the microscopic observations.

Hematolymphangioma. Presented by DR. E. A. OLIVER and DR. W. W. TOBIN (by invitation).

R. C., a girl aged 9 years, has had since birth a nodular swelling about the left elbow and numerous small red vascular lesions on the upper part of the left arm, about the left axilla and over the left side of the chest. Many deep-seated skin-colored vesicles are interspersed among the lesions. Some of these lesions are closely set, while others are discrete.

The mother states that approximately five years ago the eruption on the arm was treated with an electric needle and that for three or four months afterward there was marked enlargement of the entire left arm.

One month ago the lesions on the left side of the chest were treated with solid carbon dioxide, each lesion receiving from four to five seconds' exposure with little pressure. One week later there was diffuse enlargement and a doughy feeling of the areas treated. This enlargement presented no subjective symptoms and was not accompanied by an elevation of temperature. It has persisted to the present time.

DISCUSSION

DR. CLARK W. FINNERUD: I have never observed this complication after freezing, although I have treated a number of similar conditions with solid carbon dioxide. This marked persistent swelling apparently represents a blockage of the lymphatic vessels from acute lymphangitis.

Pemphigus Vulgaris. Presented by DR. CLARK W. FINNERUD.

C. T., a man aged 52, presented a bullous and crusting eruption of two months' duration when first seen, on Sept. 2, 1937. The first evidence of the eruption appeared during a severe "cold," which was accompanied by two days of fever. The first lesions were noticed on the nose and the back. These gradually increased in number, occurring discretely. Within a short time after the onset lesions were noticed in the mouth. The oral lesions have increased in number and of late have made eating almost impossible.

At the time of the first examination the differential leukocyte count showed 70 per cent polymorphonuclear neutrophils, 27 per cent lymphocytes, 1 per cent large mononuclears and 1 per cent transitional forms. For the past nine days the patient has had large doses of sulfanilamide, as suggested by Dr. Caro, but as yet he has shown no appreciable improvement. The blood has been checked every other day, and the erythrocytes have decreased during this treatment from 4,650,000 to 4,350,000; the leukocytes have increased from 9,700 to 17,000, and the differential count has remained practically the same. There are but 1 per cent eosinophils, and the hemoglobin has decreased from 82 per cent to 70 per cent.

DISCUSSION

DR. CLARK W. FINNERUD: I do not believe this case deserves any particular discussion, but I thought it interesting in view of Dr. Caro's recent report (ARCH. DERMAT. & SYPH. **37**:196 [Feb.] 1938) of successful treatment with sulfanilamide by the same technic. As yet this patient, given large doses, has not shown any improvement.

DR. MARCUS R. CARO: I have been using sulfanilamide in a case of pemphigus vulgaris for about four months. The dose has varied between 50 and 90 grains (3.24 and 5.82 Gm.) daily. At the beginning of treatment the patient was nearly moribund, but in about one month the skin was practically clear. The response to treatment was immediate. The patient still has a few vesicles occasionally, but these heal rapidly. Her physical condition in general is good. There has been no noticeable damage to the blood as a result of the drug, and there have been no other untoward reactions.

DR. M. H. EBERT: In view of Dr. Caro's excellent result, I think administration of sulfanilamide should be continued. I tried it in a case of typical pemphigus vulgaris at the Cook County Hospital and so far have seen absolutely no change in the condition.

DR. V. C. BELISARIO, Sydney, New South Wales (by invitation): I should like to mention something with regard to pemphigus. In 1928 I observed a case in which the involvement was severe. After using every treatment known at the time, with no response, I tried antimony intravenously, and the condition cleared like magic. In the next three or four cases, however, the medication did not have any effect.

Just before I left Sydney I had another case in which there was no response to any of the usual methods of therapy. Again I ordered the use of injections of antimony, and again the favorable effect on the pemphigus was rapid. It was only then that I realized that the two cases in which there had been benefit were instances of the vegetating type, while those in which the disease was not influenced were examples of the bullous variety. I should be interested in having others employ the drug for pemphigus vegetans. In the first case mentioned there was no recurrence of the eruption, but I cannot answer for the other two.

DR. E. MICHELSON, Minneapolis: I think that germanin has decided value in pemphigus. I by no means claim that it is a cure-all, but it is worthy of trial.

DR. RICHARD S. WEISS, St. Louis: In one case of pemphigus vulgaris my associates and I tried sulfanilamide. The patient made no progress, and treatment with tryparsamide was instituted. After the third dose he suddenly went blind and died a week or so later. Another patient was given sulfanilamide for a month and got worse. He was then given tryparsamide in large doses, and he has made satisfactory progress and apparently is in a good state of remission at present. He has slight reactions to arsenic, demonstrated by hyperkerotosis.

NOTE.—The patient died three weeks later. An autopsy was not permitted.

A Case for Diagnosis (Tropical Ulcer?). Presented by DR. F. E. SENEAR and DR. HENRY C. SCHORR (by invitation).

V. G., a Negress aged 26, presented herself on August 30 because of three oval ulcers on the anterior surface of the right leg. The ulcers were deep and had a granulomatous base. The edges were ragged and showed little tendency to heal. She states that she recently returned from the Philippine Islands and that she had injections of arsphenamine two months ago.

She had a statement from the ship's physician and others familiar with such lesions that during her voyage she was treated for these ulcers and that they had been diagnosed tentatively as tropical ulcers.

Direct smears showed Donovan bodies. A piece of tissue was clipped off the edge of the ulcer for histologic examination. The Wassermann and the Kahn reaction were negative.

A direct smear was sent to Tulane University, and the report was: "Many pathogenic cocci but no Donovan bodies were found."

The report of the histologic examination by Dr. M. R. Caro was as follows: "The epidermis showed acanthosis and intercellular edema. In one place was an ulcer filled by granulation tissue and containing many pus cells, lymphocytes and erythrocytes.

"The corium was edematous. The blood vessels had thickened walls, and there were many newly formed vessels, surrounded by densely packed infiltration of pus cells, plasma cells, macrophages and lymphocytes. There were much free blood and blood pigment throughout the tissue.

"No Donovan bodies were found."

DISCUSSION

DR. WILLIAM A. ROSENBERG (by invitation): The patient told me about having diarrhea first and the ulcer following the diarrhea. She has had repeated attacks of diarrhea since then. I wonder if the condition is not uncinariasis. She comes from a country where it may be expected.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: The ulcers of the legs appear ecthymatous, and at least for the present they are without the characteristics of the ulcers which have been reported in association with amebiasis or with chronic ulcerative colitis.

DR. RALPH H. SCULL (by invitation): Dr. Nomland suggested that I mention those cases of sickle cell anemia which he observed with me in which ulcers on

the lower extremities were not unlike those seen in this case. These ulcers, described by Huck (*Bull. Johns Hopkins Hosp.* **34**:335-344 [Oct.] 1923) and others, resemble those of syphilis on the shins and the ankles and have a punched-out appearance.

A Case for Diagnosis (Prurigo Nodularis?). Presented by DR. F. E. SENEAR and DR. MINNIE O. PERLSTEIN.

M. T., a Negress aged 42, presents an eruption of more than twenty-two years' duration. She states that the present eruption apparently came on during an epidemic of some generalized pruritic disease which affected most members of the community in which she lived. The eruption has not varied since its onset, although there are periods of exacerbation, and rarely one or more lesions apparently undergo spontaneous involution. Various types of local medication have produced no relief. There is apparently no seasonal influence. The patient's general health has been essentially good, except for a hysterectomy six years ago. During the past five months a diagnosis of grade 2 carcinoma of the cervical stump has been made, and the patient has received fifteen treatments with high voltage roentgen rays.

The eruption consists of bilateral and roughly symmetrical lesions over the extremities, most accentuated on the extensor surfaces. The lesions themselves are firm nodules, vary in size from that of a pea to that of a dime, and show no tendency to coalesce. The larger lesions are rough, and some present a hemorrhagic summit. The skin surrounding the lesions is hyperpigmented and lichenified. There is a marked urticarial tendency of the entire skin, and smaller nodular lesions are scattered over the trunk. General physical examination showed no abnormality except for the aforementioned malignant growth.

Histologic examination showed: acanthosis of the epidermis and lengthening of the rete pegs. There was scattered intracellular edema; the granular layer was discontinuous, and there was a thick parakeratotic scale.

The blood vessels in the upper part of the corium were dilated and were surrounded by circumscribed mantles of cellular infiltration composed largely of lymphocytes and macrophages, with a few eosinophils. In the upper part of the corium the collagen fibers were edematous and swollen, while the elastic fibers were gone.

DISCUSSION

DR. M. H. EBERT: I have seen this woman in the hospital. The picture does not fit my idea of prurigo nodularis. I think it is lichen corneus hypertrophicus, which is different. The patient had generalized pruritus; she presents other areas in which the involvement is not nodular but is of the type of lichen simplex chronicus. In addition, the lesions come and go. In prurigo nodularis the lesions are discrete and persist indefinitely. If excised they recur in the same area, and there is no acute exacerbation as there is in this case. I should call this case one of lichen corneus hypertrophicus rather than of prurigo nodularis.

DR. H. E. MICHELSON, Minneapolis: I did not think that this condition was prurigo nodularis when I examined the patient, but I must admit that the microscopic section is characteristic of that condition. Since little is known about the etiology of nodular pruritus as described by Hyde, there is no reason why a variant such as that shown today cannot exist.

DR. F. E. SENEAR: I am glad to have the discussion of Drs. Ebert and Michelson. We were open minded, because the skin seems to have the peculiar predilection for lichenification often remarked in chronic dermatoses among Negroes. The condition did not fit in with typical prurigo nodularis. However, the marked hypertrophy and the conformity of the individual lesions with those of prurigo nodularis made us feel much as Dr. Michelson does, that the condition is not necessarily a sharply defined picture, and the case was presented with a question.

Darier's Disease. Presented by DR. F. E. SENEAR.

This boy, C. T., had patches of dermatitis in the temporal region at the age of 6 years. These gradually spread during several years until the entire scalp, the forehead, parts of the face, the trunk (especially the interscapular and the sternal region) and the forearms were involved.

The patient states that the condition improves almost to the point of disappearance during the winter, with exacerbations in the spring.

A similar but much more extensive condition developed in his mother when she was 13 years old and has persisted till the present time—a duration of forty years. Until eight years ago the condition was present only in the summer, but since then it has been present in the winter as well.

The patient has one brother and three sisters. One sister has a similar condition involving the scalp, the neck, the shoulders and the genitalia, while another sister shows involvement of the scalp and the interscapular region. The other sister and the brother are not affected.

DISCUSSION

DR. RICHARD S. WEISS, St. Louis: There is no question as to the diagnosis in this case. It is rather striking that the eruption occurs only in the summer. I recall one and perhaps two cases with that history.

DR. F. E. SENEAR: When this case was mentioned at Rochester, Minn., last year, Dr. O'Leary said he had observed this intensity in summer and recession in winter in several cases. I have not seen any mention of this seasonal variation in the textbooks, and I think it is particularly striking that in the cases at the Mayo Clinic, as well as in those in this family, there is a notable seasonal incidence.

Xanthoma Diabeticorum. Presented by DR. S. J. ZAKON (by invitation) for DR. A. W. STILLIANS.

K., a Jewish housewife aged 66, states that during the past two years she has noticed nodules on the extensor surfaces of her arms and legs. There have been no subjective symptoms. Examination on Aug. 20, 1937, at the dispensary of the Mount Sinai Hospital showed her to be a well nourished elderly woman with lesions on both elbows, the external surface of the right thigh, the extensor surfaces of the arms and the forearms and the left thigh. The lesions on the elbows are soft brown-red papules and nodules, grouped in circles, sharply demarcated and with a depressed center and an elevated border.

The other lesions are discrete papules and plaques. Over some of the papules dilated capillaries are seen. Urinalysis showed much sugar and some acetone. The sugar content of the blood was 320 mg. per hundred cubic centimeters.

Histologic examination showed marked hyperplasia of the connective tissue and numerous xanthoma cells.

DISCUSSION

DR. CLARK W. FINNERUD: I want to ask about the diagnosis, because frequently patients with the tuberous form of xanthoma have the same urinary findings. Are the lesions limited to the elbows in this case?

DR. RICHARD S. WEISS, St. Louis: I took this case to be one of xanthoma tuberosum multiplex.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: A study of xanthoma is interesting because of the not uncommon association with hyperlipemia and cardiovascular disease, and this association may be present even with localized types of lesions, such as xanthoma palpebrarum. Last week I saw a woman aged about 50 years whose chief complaint was angina pectoris; she had a few small xanthomas on the lower eyelids. There was no glycosuria, and she was not obese. However, examination of the blood revealed the lipoids to total 1,200 mg. per hundred cubic centimeters, which is almost double the normal quantity.

Sarcoid (Besnier-Boeck-Schaumann Type). Presented by Dr. M. H. Ebert.

C. R., a youth aged 19, presents an eruption of approximately one year's duration which causes no sensation. He has noticed enlarged glands in the groin for about the same length of time.

The eruption is fairly generalized, more marked on the face, the extensor surfaces of the arms, the buttocks, the back and the lower extremities. The individual lesions consist of pinkish nodules, varying in size from that of a match head to that of a bean. They are infiltrated and slightly raised. Many of them are grouped in irregular patches, especially in the region of the triceps. On the face they are most noticeable on the nose. Under diascopic pressure a brownish discoloration remains, which is punctate at the margin. The lymphatic glands over Hunter's canal on either side are the size of a hen's egg. There are several almond-sized glands in either inguinal region and in the axillae and bean-sized glands in the submaxillary, the postauricular and the cervical region. These glands are painless and movable. There are no lesions of the mucous membrane.

A roentgenogram of the chest shows increased hilar markings, with fibrosis extending throughout the parenchyma. The reaction to the Mantoux test was negative with dilutions of tuberculin of 1:1,000 and 1:100. The Wassermann reaction was negative. A smear of blood showed nothing of significance

Histologic examination showed well defined areas of cellular infiltration extending from the subpapillary zone the entire depth of the corium. Many of these groups were arranged in strands. They were made up of epithelioid cells with a few lymphocytes at the margin. There was no evidence of reaction in the surrounding corium.

DISCUSSION

Dr. H. E. Michelson, Minneapolis: I am happy to have had the privilege of seeing this patient. Rarely is it possible to see such a classic example of the syndrome which is now being called Besnier-Boeck disease. It is interesting in passing to note that Hutchinson described features of this disease before Caesar Boeck. Gradually it is being realized that the entire group of symptoms under this head have been recognized for many years but have not been grouped under a single name.

Dr. Clark W. Finnerud: As Dr. Ebert pointed out, the nests are large and deep-seated and consist exclusively of epithelioid cells. The structure is similar to that of lupus pernio. Only in old lesions of that type have I seen such nests of epithelioid cells, practically no connective tissue or cellular infiltration of lymphocytes or plasma cells being present.

Dr. M. H. Ebert: This disease is referred to as a variety of reticuloendotheliosis, and it is interesting that the lungs were involved, the lymphatic vessels were enlarged and the spleen was markedly enlarged. Unfortunately I did not have the opportunity to make a roentgenographic study of the bones to see if there was osteoporosis. I did make a blood smear. There was an increase of the monocytes. Further study will be made in this case.

A Case for Diagnosis (Dermatitis Vegetans?). Presented by Dr. Theodore Cornbleet and Dr. Earl R. Pace (by invitation).

C. H., a woman aged 82, first noticed the peculiar changes in the skin of her legs two years ago. She does not remember how they started. The skin shows a peculiar warty, vegetative translucent thickening, which differs from dermatitis vegetans in its great extent, symmetry, translucence and hardness. There is no pain when the patient rests in bed, but pain is present when she is standing. The changes involve the entire lower extremities up to the knees.

Urinalysis showed a specific gravity of 1.018, no albumin and no sugar. The congo red test for amyloid gave negative results.

DISCUSSION

Dr. E. P. Zeisler: I have seen a similar condition in patients with cardiac decompensation who were unable to lie down. As a result of the stasis and edema

of the legs, a vegetative dermatitis occurs. The clinical picture in this case is extraordinary and corresponds to that of verrucous eczema.

DR. M. J. REUTER, Milwaukee: I think the condition is dermatitis vegetans secondary to stasis in a person who has been neglectful of herself.

DR. DAVID LIEBERTHAL: This condition is so-called verrucous eczema. I have found hot sitz baths and wet dressings of mild astringent solutions beneficial in the few cases which have come under my observation.

Poikiloderma Atrophicans Vasculare. Presented by DR. S. J. ZAKON (by invitation) for DR. A. W. STILLIANS.

E. B., a Jewish housewife aged 47, has been ill since 1916. At that time she had an attack of typhus, and since then she has complained of headaches and an eruption. At first only small circumscribed areas of the body were involved; at present there is almost universal involvement. The skin is dry, red, mottled, scaly and atrophic, with numerous fine telangiectases and petechiae.

At times she complains of burning of the skin more than pruritus and muscular soreness. In the last few weeks erosions and ulcerations have occurred in the region of the breasts.

A roentgenogram of the head showed no abnormality except for a large calcified pineal gland. That of the chest showed old healed tuberculosis of the apex of the right lung. The results of all examinations of the blood have been within normal limits.

Dr. Montgomery, who studied the microscopic section of a biopsy specimen which was taken in May 1937, is of the opinion that the picture was confirmatory of the clinical diagnosis of poikiloderma atrophicans vasculare.

DISCUSSION

DR. A. W. STILLIANS: The case was presented because of the extensive involvement.

Naevus Albus. Presented by DR. CLARK W. FINNERUD and DR. RALPH H. SCULL (by invitation).

E. J., a Negress aged 35, presents lesions of the back and abdomen, which have been present all her life. There have been no subjective symptoms and no change in the size or the shape of the cutaneous lesions.

Examination shows a broad band of partial macular depigmentation over the chest, the abdomen and the back.

A section of the border between the normal and the partially depigmented skin, stained with hematoxylin and eosin and with silver nitrate, showed no apparent change in the number or the size of the blood vessels but merely a decrease in pigment in the grossly lighter colored skin.

DISCUSSION

DR. CLARK W. FINNERUD: We thought the lesion was a white nevus. We found the same amount of vascular reaction to rubbing with ice in the pigmented as in the depigmented skin. Biopsy showed approximately the same number and size of blood vessels in the deeply pigmented portion as in the depigmented or partially pigmented portions.

DR. S. W. BECKER: The lesion is not completely depigmented; it simply shows a tendency in that direction. I think it is a lesion of prenatal origin.

DR. CLARK W. FINNERUD: I showed a Negro family with partial albinism some years ago, and some of the members may remember that the lesions occurred in approximately the same area in all generations. Each one had a dollar-sized area on the forehead, extending into the hair. The extensive distribution in the case presented today is interesting, both sides of the trunk, the front and the back being involved.

OTTO H. FOERSTER, M.D., *President*

Nov. 17, 1937

H. RATTNER, M.D., *Secretary*

Steatocystoma Multiplex. Presented by DR. WILLIAM A. ROSENBERG (by invitation) for DR. A. W. STILLIANS.

H. S., an American-born Chinese aged 21, states that the present condition began with an eruption on the chest and the abdomen five years ago. The lesions, which were few at first, gradually increased and at the present time are numerous.

Examination on Nov. 4, 1937, showed an eruption on the chest and the abdomen which consisted of papules and nodules varying in size from that of a pinhead to that of a pea and larger. The lesions are round or oval, of the color of normal skin, soft and painless. Puncture of several of the lesions caused a thick milky white fluid to exude. There are no subjective symptoms.

Histologic examination showed a picture compatible with the diagnosis of steatocystoma multiplex.

DISCUSSION

DR. OLIVER S. ORMSBY: I think this case presents the classic features of that disease. Dr. Finnerud and I reported the first case in this country, and in that case the prediction made at that time, that when the cyst was completely emptied it would not be reproduced, has been fulfilled. During the last seven years Dr. Ebert has incised and removed the contents of over 2,000 cysts on that patient, and there has been practically no recurrence of lesions so treated.

DR. CLARK W. FINNERUD: It was conspicuous in the literature, when I went over the previously recorded cases, that most of the patients had no associated disease of the sebaceous glands. Acne was mentioned specifically. Possibly this is because most patients were beyond the usual age for acne. The patient presented today had mild acne vulgaris of the face, as did another patient with steatocystoma multiplex whom I have seen within the last few months.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I agree with the diagnosis. The histologic picture is that of an epithelial rather than a sebaceous cyst. It duplicates the histologic picture of solitary epithelial cysts which may occur on any part of the body. These epithelial cysts form stratified epithelium rather than sebaceous or sweat gland cells, and this explains the different character of their fluid content and the different response to therapy.

DR. OLIVER S. ORMSBY: I wish to state, if Dr. Montgomery refers to the type of cyst reported by Drs. Wien and Caro and by Drs. Taussig and Allington, that the lesions were found on the palms and the palmar surfaces of the fingers. They were all epithelial cysts and differed from sebaceous cysts.

DR. CLARK W. FINNERUD: Dr. Ormsby and I made serial sections in the cases we reported, and we found remnants of atrophic sebaceous glands in the wall of the cyst, so I believe the cysts to be composed of both duct and gland elements.

DR. S. W. BECKER: I have had some difficulty in microscopic diagnosis; I do not mean with patients with generalized eruptions such as this. A diagnosis of sebaceous cyst is usually made, but in histologic section sebaceous glands may or may not appear in the wall. If their presence is established, the condition is sebaceous cyst; otherwise, the diagnosis is epidermoid cyst. So the only way to be sure is to do as Dr. Finnerud said, make serial sections.

DR. MARCUS R. CARO: Dr. Wien and I reported (Traumatic Epithelial Cysts of the Skin, *J. A. M. A.* **102**:197 [Jan. 20] 1934) three cases of traumatic epithelial cyst of the skin, produced by the implantation of bits of epidermis in the deeper tissues through injury. In one of the cases in which we were able to make histologic study the epithelial lining of the cyst took on the same characteristics

as those of the outside epidermis and showed considerable cornification. Such a lining is entirely unlike that seen in lesions of steatocystoma.

DR. OLIVER S. ORMSBY: The contents of the larger cysts in the type of case presented today are so different from what is found in the ordinary sebaceous cyst that this ought to be stressed. The material is liquid and resembles olive oil in color and consistency. In the smaller lesions ordinary sebaceous material is usually found.

DR. A. W. STILLIANS: I hoped that Dr. Ormsby would mention the odorlessness of this material. That strikes me as most peculiar. The odor usually noted in sebaceous material is entirely lacking.

Lichenoid Dermatitis Resembling Amyloidosis. Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

W. B., a man of German-American stock, aged 49, complained of a pruritic eruption of the lower part of the left leg of twenty-four years' duration. It began as a "red spot," gradually spread and then remained the same. He has had diabetes for three years. On physical examination he was found to have general arteriosclerosis. The blood pressure was 140 systolic and 85 diastolic; the Wassermann and the Kahn reaction were negative. The basal metabolic rate was —14 per cent. The dextrose content of the blood was 127 mg. per hundred cubic centimeters. The blood count showed no abnormality. Urinalysis showed occasional traces of sugar.

Examination revealed a plaque on the left shin of about 10 by 8 cm., consisting of a conglomeration of flat papules which were slightly elevated, firm, pale pink and somewhat translucent.

The clinical picture seemed so typical for lichenoid, local amyloidosis that congo red was injected intracutaneously at once to confirm the diagnosis. The lesions, however, failed to take the stain. Likewise, it was impossible to demonstrate amyloid in the biopsy specimen, which showed changes typical of lichen simplex chronicus.

DISCUSSION

DR. E. P. ZEISLER: Lichen simplex chronicus on the legs may show obtuse papules, become rather hypertrophic and simulate localized amyloidosis. The histologic examination is the deciding factor.

DR. M. J. REUTER, Milwaukee: I think practitioners are becoming so conscious of localized amyloidosis that we hesitate to make a diagnosis of lichen simplex chronicus without a biopsy.

DR. S. W. BECKER: We presented this patient because there was some argument as to what is called localized amyloidosis. Some argue that the condition is lichenified dermatitis with secondary amyloid. Here is a man who has had this lesion for many years and shown no signs of amyloidosis microscopically.

DR. M. E. OBERMAYER: In connection with Dr. Finnerud's statements, I should like to point out that there is no scaling in localized amyloidosis or in a condition resembling it; the papules retain their smooth surface and somewhat translucent appearance throughout. Even if it is assumed that our case represents only a peculiar variety of lichen simplex chonicus, this point deserves attention, because it makes clinical differentiation possible.

Pityriasis Rubra Pilaris. Presented by DR. CLARK W. FINNERUD and DR. W. W. TOBIN (by invitation).

This patient, a girl aged 4 years, had a diffuse, dry, scaly, reddened inflammation of the palms and the soles of two years' duration. The mother states that new areas gradually developed on the front parts of the ankles, the backs of the hands, the elbows, the knees, the face and the scalp.

The entire surfaces of the palms and the soles have a sharply marginated diffuse, scaling, reddish thickening. There are similar psoriasiform or keratoderma-like infiltrations on the elbows, the knees and the dorsa of the feet and the fingers. On both knees are closely set scaling acuminate papules, which have a typical "nutmeg-grater" effect when rubbed. The scalp is dry and the hair lusterless, and there is a fine powdery scaling through it and on the nose and the cheeks. There are no conical papules on the dorsa of the fingers.

Serologic tests were negative, and a roentgenogram of the chest showed no abnormality.

DISCUSSION

DR. E. A. OLIVER: This case was presented by me at the clinic two weeks ago as a case of pityriasis rubra pilaris. It lacks a few of the classic symptoms of that disease, such as the small, horny black papules on the dorsal aspects of the fingers and the seborrhea of the face and the scalp, but the presence of the palmar and plantar hyperkeratosis and the isolated plaques on the extensor aspects of the lower parts of the legs and the forearms make this diagnosis the most probable one. The picture is, however, slightly atypical.

DR. WILLIAM ALLEN PUSEY: I should like to know how this condition is differentiated from the old symmetrical keratoderma of the extremities. Clinically the patient presents a classic picture of that disease. It is certainly not to me a typical picture of Devergie's disease. The absence of characteristic papular horny plugs in the skin on the backs of the fingers makes uncertain in my mind a diagnosis of Devergie's disease, regardless of the histologic picture.

DR. F. E. SENEAR: I believe the case is one of symmetrical keratoderma. I have observed a few cases of pityriasis rubra pilaris in which the picture was entirely in keeping with symmetrical keratoderma at first. In the absence of any follicular lesions and of involvement of the phalanges, I think one should have to wait until some other characteristics did develop before one could accept this case definitely as one of Devergie's disease.

DR. JAMES H. MITCHELL: I am pleased to find that Dr. Pusey is running true to form, in view of the fact that he did not accept my diagnosis in a case I presented at the annual Meeting of the American Dermatological Association in 1933. The picture in that case was much like this. At that time I promised to eat crow with him if the case did not turn out to be one of pityriasis rubra pilaris. The condition was similar and the patient a girl of about the same age.

DR. E. P. ZEISLER: A good many years ago I wrote a paper on Devergie's disease, particularly in children (Pityriasis Rubra Pilaris—Familial Type, ARCH. DERMAT. & SYPH. **7**:195 [Feb.] 1923). Of the group of cases I reported, there was one in which the patient was the father of three children and had been a patient of my father many years ago. He was told that the condition was not hereditary and that it was safe for him to marry, and typical Devergie's disease, with changes in the nails, hyperkeratosis of the palms and soles, scaling on the scalp and psoriasiform plaques on the elbows and knees developed in the three children. It never became universal as it sometimes does. It was extremely chronic, and the clinical picture was the same as in the case presented today. I think the picture of Devergie's disease must be recognized to be variable. There are an acute spreading type in adults, which becomes almost universal, and a chronic type in children, which resembles symmetrical keratoderma.

DR. THEODORE CORNBLEET: Last year I presented before this society a 1 year old child who had a similar eruption. In that case there was erythroderma of the palms and soles, which spread to the backs of the hands and the dorsa of the feet, and there were distinct psoriasiform lesions on the elbows and elsewhere. The diagnosis lay between psoriasis and Devergie's disease, but the consensus favored the latter. The appearance of the palms and soles of the present patient is strikingly similar to that in the case I presented.

DR. CLARK W. FINNERUD: All the cardinal symptoms of pityriasis rubra pilaris are here, except follicular keratosis on the backs of the fingers and elsewhere. A similar clinical picture was presented by a patient in Dr. Oliver's and my service at the Children's Memorial Hospital years ago, and characteristic follicular papules later developed.

Blastomycosis of the Nasal Septum. Presented by DR. M. H. EBERT.

I. L., a woman aged 21, first noticed what appeared to be a cold sore on the upper lip seven months ago. This was treated by the local druggist and seemed to become infected. Later it was cauterized by her physician, but it rapidly increased until it was the size of an olive. Since that time it has been treated by roentgen therapy. She has had 20 roentgen treatments in all. The original lesion was absorbed, but the process extended to the nasal septum, where it has been growing rapidly. Her family and personal history are irrelevant.

There is a raised papillomatous mass extending along the cutaneous portion of the nasal septum down onto the upper lip. This is covered with a heavy crust. When the crust is removed, droplets of pus exude from between the papillae. The margin is dull red and drops abruptly to the surrounding skin. There is a shallow scar of the early lesion on the upper lip. The Wassermann reaction was negative. The Mantoux test with old tuberculin in a dilution of 1:100 gave a negative result.

Histologic examination showed a marked and irregular acanthosis, with numerous micro-abscesses in the epidermis. There was nonspecific granulation tissue in the corium and a few giant cells. Budding double-contoured blastomycetes were easily found in the micro-abscesses. Similar organisms were recovered in preparations of fresh pus in potassium hydrate.

DISCUSSION

DR. H. R. FOERSTER, Milwaukee: I consider this case worthy of discussion because of its unusual clinical features. The location of the eruption at a mucocutaneous border is uncommon for blastomycosis, and the characteristic features of inflammatory margin, verrucous surface and miliary abscesses are absent or not clearly defined. The demonstration of the blastomycetes in the histologic section as the proof of the presenter's clinical diagnosis is noteworthy.

DR. OLIVER S. ORMSBY: I should like to concur in that. Clinically the lesion resembles either hypertrophic lupus vulgaris or a bromide eruption, rather than blastomycosis. There is no inflammatory margin containing the miliary abscesses of blastomycosis. Therefore, it was impossible to get material for microscopic examination. The organisms were readily demonstrable, as were microscopic miliary abscesses, in the histologic sections, which naturally settled the diagnosis.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I have observed several cases of blastomycosis involving the mucocutaneous junctions. When it occurs in these areas, one may not see the typical border with miliary abscesses. The lesion more closely resembles bromoderma or even ordinary pyoderma or furunculosis. The typical organisms, however, in my experience, can be demonstrated readily, even in these clinically atypical lesions of blastomycosis.

DR. S. W. BECKER: This discussion reminds me of a statement made by Bloch that in Europe they call this condition tuberculosis verrucosa cutis because they do not use the term blastomycosis. About two years ago I had a patient with a vegetative lesion on the thumb which was typical for tuberculosis verrucosa cutis. There were no miliary abscesses in one half of the specimen. There were giant cells with tuberculoid tissue. There were some miliary abscesses with blastomycetes in the other part of the specimen, but there were no gross abscesses, and the lesion was atypical for blastomycosis.

DR. JAMES H. MITCHELL: Two years ago I presented a patient who had a lesion on the buttock. It was assumed by all to be verrucous tuberculosis. There

was no miliary abscess at all. There was a little crusting, but beneath the crusts the pus could be expressed in small droplets, in which the organisms were numerous. Cultures were readily obtained and were demonstrated with the patient.

DR. M. H. EBERT: I agree with all the speakers that a little overconfidence in diagnosis is likely. This locality being the center for blastomycosis, dermatologists in this area think they can recognize the condition on sight. The present case is an illustration of the fact that blastomycosis is occasionally atypical, indicating further search as well as biopsy. Another reason for showing this case is the matter of treatment. This patient has had twenty or more roentgen treatments to this area. I mention it because it is known that roentgen radiation makes a good adjuvant at times in finishing up treatment carried on with potassium iodide. This is a good illustration of the fact that roentgen therapy alone will not effect a cure.

A Case for Diagnosis (Seborrheic Psoriasis?). Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

M. T., a girl aged 7 years, presents a pruritic eruption which began behind the ears at the age of 9 months and rapidly became generalized. Since that time she has had remissions, but in general the eruption has persisted. Because of her condition the girl has not yet started school. At one time, according to the parents, "large blisters" developed, the contents of which had an offensive odor. She was taken to the Children's Memorial Hospital, but no benefit followed hospitalization. The parents brought her to the Research and Educational Hospital, where the condition cleared within one month, only to recur immediately after discharge. She was readmitted and stayed three months without experiencing improvement. At that time there was considerable oozing from the lesions; her scalp was severely affected, and there was loss of hair over the vertex. A year of ambulatory treatment by a private physician brought considerable improvement, but the condition recurred soon. No seasonal differences could be observed.

Her family history revealed no pertinent facts. There were no cutaneous or allergic diseases in the family.

She was admitted to the Billings Hospital in March 1936. Physical examination showed no abnormality except enlarged tonsils. Laboratory examination showed no abnormality in blood or urine. At the time of admission she presented a generalized psoriasiform eruption. The lesions were erythematous, of the color of seborrheic eczema and covered with fine dry scales. The scalp and the face were diffusely involved. She was hospitalized for seven weeks. During this time tonsillectomy and adenoidectomy were performed. She was repeatedly examined by a psychologist and was classified as of borderline inferior intelligence (Stanford-Binet quotient, 65-78).

Under routine management for psoriasis the skin improved steadily. The condition of the scalp, however, remained intractable, became exudative and had a putrid odor. When she was discharged, after seven weeks' hospitalization, her skin was practically clear, but her scalp was still erythematous. She was readmitted in May 1936, with a recurrence involving the upper part of the body and seeming to have descended from the scalp. Her hair had fallen completely. Her scalp was again oozing a fetid exudate. Roentgen irradiation of some areas was added to the routine management, and a number of local applications were tried without effect. In September pustules appeared on the scalp. In October chronic external otitis developed. For a considerable time she was given daily injections of moccasin venom in a dose of 0.05 cc. of a 1:3,000 solution. The effect was doubtful. However, her hair started to grow again and reached normal thickness. In April, after eleven months' hospitalization, the patient was discharged because of an outbreak of varicella in the ward. She was readmitted in May. At that time her scalp and face were diffusely involved and showed oozing and crusting, while the rest of the lesions retained their psoriasiform character.

During the summer the patient was seen once by Dr. Stillians in consultation. She has since been in the hospital and has had slight remissions and exacerbations.

Histologic examination showed hyperkeratosis and parakeratosis, a thickened stratum mucosum with prominent intercellular bridges, intercellular edema and broad, flattened rete pegs. A few of the papillae were elongated, extending close to the surface. The papillary and the subpapillary layer of the corium showed a perivascular round cell infiltrate. There was some degeneration of collagen. It was felt that the histologic picture was compatible with psoriasis.

DISCUSSION

DR. F. E. SENEAR: According to the history, the girl was in the Research and Educational Hospital some time ago. I do not remember the details of her visit there. As I see the picture today, I should think it was not that of a seborrheic form of psoriasis but rather that of a form of seborrheic eczema. I rather vaguely recall that when the patient was under my observation there was some suggestion of the picture of pityriasis rubra pilaris.

DR. OLIVER S. ORMSBY: I think it is instructive to follow the progress of a patient like this over a period of years. I have seen patients whose records showed a predominance of symptoms of psoriasis at one time and of seborrheic eczema at another. This patient now presents the clinical picture of seborrheic eczema. While the photograph shown today suggests psoriasis, it illustrates the fact that there is a clinical type in which a distinction between the two conditions is difficult to make. This type is resistant to treatment. Whether this patient has a borderline condition or an independent one remains to be proved.

DR. WILLIAM H. GOECKERMAN, Los Angeles (by invitation): I should lean more to a diagnosis of psoriasis than to one of seborrheic eczema. While I was examining the patient, Dr. Becker was twitting me about my tar treatment, and I told him he had not applied the proper technic. I am fully in accord with what Dr. Ormsby has said. I think these borderline conditions are common, and they do vary at times. In this particular case, however, with this microscopic picture, I feel that a diagnosis of psoriasis should be maintained. If the history is correct, the early onset is peculiar.

DR. WILLIAM ALLEN PUSEY: At first sight I was struck by the appearance of ichthyosiform erythroderma in this case. The glossy red dermatitis of the face and neck, as far down as the upper third of the sternum, makes the clinical picture of that condition. The intractability to treatment is also characteristic. Fred Harris used to say that seborrheic eczema was the rheumatism of dermatology, meaning by that that the dermatologists were giving that name to all sorts of things of which they were not certain. I think there is a tendency now to use psoriasis in the same way in connection with obscure scaly dermatoses. The present condition I believe to be erythroderma ichthyosiforme, which is essentially a hereditary defect in the skin.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I am in entire accord that it may be difficult in certain cases to differentiate between psoriasis and seborrheic eczema either clinically or at times even histologically. In this case clinically the pitting of several of the finger nails and the scaling beneath others would strongly suggest psoriasis, and the biopsy specimen shows all the histologic changes characteristic of psoriasis. It does not show the histologic features of ichthyosiform erythroderma.

DR. THEODORE CORNBLEET: When this patient was studied several years ago at the Research and Educational Hospital, the lesions were more vividly colored and more thickened. A striking change is the disappearance of a marked ectropion which was present at that time. As regards a possible diagnosis of congenital ichthyosiform erythroderma, there was little change in the folds, as I recall, nor were any bullae present at that time. I think my associates and I leaned toward the diagnosis of Devergie's disease.

Dr. Clark W. Finnerud: At one time, when I was taking many cultures in cases supposedly of seborrheic eczema, I practically came to the conclusion that there was no such entity. I once heard Dr. Mitchell express that opinion, and I therefore should be interested in hearing his discussion of this case.

Dr. James H. Mitchell: I dislike being put on the spot in this way. Of one thing I am convinced, and that is that seborrheic eczema about the ears may be of streptococcic origin. Many of my colleagues do not believe that may be true. Nevertheless, seborrheic eczema is definitely an entity, in my opinion. There is, of course, seborrheic eczema in the scalp and on the glabrous skin associated with Pityrosporon ovale. When that organism is present, the dermatitis has characteristics different from those of the dermatosis in which streptococci appear.

Dr. William H. Goeckerman, Los Angeles (by invitation): I essentially agree with Dr. Mitchell, not that there is no seborrheic eczema, but that many times lesions which have been called seborrheic present a distinctive picture. To me they appear to have a serous oozing, as contrasted with the exudation of an oily material. Notwithstanding, they give one a feeling of extreme dryness. Yet they impress one as being seborrheic eczema. I have in recent years treated them as streptococcic infections, and my results have been much better than before. In other words, I think there is a type of seborrheic eczema which is probably due to the streptococcus with an allergic factor involved. Under treatment with mild antiseptic preparations the condition, I think, does well.

Dr. E. P. Zeisler: As long as so many diagnoses have been suggested, I should like to add chronic moniliasis of the skin.

Dr. E. A. Oliver: This case, I believe, is one of seborrheic eczema. My experience has been limited to several cases in which young adults were involved. In these the condition was of streptococcic origin. It is difficult to treat successfully. I agree with Dr. Goeckerman that the best results are obtained with mild antiseptic solutions and mild ointments. I have had good results in young adults with vaccine therapy. The successful treatment of this child offers a considerable problem.

Dr. S. W. Becker: I appreciate the discussion. We made repeated cultures for Monilia and were unable to find any. We have treated the condition as an infection, with several different antiseptic preparations. We had successful initial results from Dr. Goeckerman's crude coal tar and ultraviolet ray technic, but since then the recurrences have been of the exudative type and have not responded.

A Case for Diagnosis (Lymphoblastoma?). Presented by Dr. H. Shellow (by invitation).

H. V., a man aged 35, states that he has had an eruption for almost four years. It started along the spinal column at the point of contact on the back and later spread to other portions of the back, to the sides and to the front of the chest. From time to time the eruption became more pronounced and raised and then subsided to an almost imperceptible pinkish color. It has never been pruritic or caused any subjective symptoms. After a course of ultraviolet ray treatment, the eruption disappeared for many months and then recurred. No change was noticed in the skin in areas in which the lesions had been. The patient states that his general health has been uniformly good, except for the occurrence from time to time of rosacea on the nose and a follicular pustular eruption on the inner surfaces of the thighs last year, which promptly disappeared under treatment. At 7 years of age he underwent an operation for the removal of tuberculous glands of the neck.

Examination reveals a well nourished man with an eruption on the front, the back and the side of the chest, consisting of pea-sized and larger papules grouped in patches varying in size from that of a quarter to half that of a palm. A few of the patches are distinctly annular and show normal skin in the center. The

edges of the lesions seem to fade gradually into the surrounding skin. The lesions are firm, and the color does not completely disappear under firm diascopic pressure. Dermographism is not present. There are a few rosaceaform papules on the nose and the cheeks. Except for a palpable lymph gland in each axilla, there is no adenopathy.

Histologic examination showed no changes in the epidermis and the papillary layer. Throughout the rest of the corium there were sharply circumscribed thick mantles of densely packed cells about all the blood vessels, the sweat glands and the sebaceous glands. This infiltration was composed almost entirely of lymphocytes, with a few reticulo-endothelial cells, and was present also within the walls of the vessels.

Examination of the blood showed nothing abnormal.

DISCUSSION

DR. OLIVER S. ORMSBY: I do not believe it possible to make a positive diagnosis, but I think that erythema perstans can be ruled out. The lesions are more plaquelike, nodular and deep than those in any of the four varieties of erythema perstans. Syphilis can be excluded readily by the persistence of the lesions without change over so long a period. That leaves only an unidentified granuloma, probably some form of lymphoblastoma.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The histologic picture reveals a dense infiltrate of lymphocytes, with occasional evidence of mitotic cell division. This is definitely a picture of lymphoblastoma, but it is not specific as to the type of lymphoblastoma. Clinically, it is not unusual for lymphoblastoma to start out with lesions which resemble erythema multiforme or urticaria but present a greater degree of induration and may not undergo complete involution. The arciform arrangement of the lesions in this case suggests mycosis fungoides. The histologic picture would fit in better with so-called Spiegler-Fendt sarcoid, which is essentially a low grade type of lymphoblastoma.

DR. FREDERICK R. SCHMIDT: I feel that there is too much infiltration in these lesions to justify fitting them into the group of erythema, and I have seen lesions of this character which were not lymphoblastoma. There is a tendency at present to call such lesions benign lymphocytoma. I have seen lesions of this character on the face that have persisted over five years, with disappearance and recurrence, and the picture under the microscope resembled that seen here. Dr. H. Fuhs, of Vienna, Austria, classified them as benign lymphocytoma. I see that more cases of this condition are being reported.

Gummatous Syphiloderm of the Malignant Type. Presented by DR. M. H. EBERT and DR. EDWARD A. SKOLNIK.

L. R., a man aged 28, states that three years ago he had a sore throat and an eruption all over his body. He received only local treatment for the sore throat, and no serologic test of the blood was made. The present trouble began about nine months ago with the development of cutaneous lesions on the lower part of the body posteriorly. Soon thereafter lesions developed on the left thigh and extended to the knee. The patient states that he has not had primary syphilis.

At the age of 12 years he had rheumatic fever, chorea and diphtheria. About twelve years ago he had a recurrence of rheumatic fever. Since then he has had palpitation of the heart.

Examination discloses two large scars on each side of the body, with the typical configuration of disappearing gummatous lesions, and active lesions on the left thigh extending to the knee, with the same typical configuration, nodular borders and destruction in the center, from which a gummatous fluid exudes.

Cardiac examination showed enlargement of the heart to the left; presystolic, systolic and diastolic murmurs at the apex and systolic and diastolic murmurs in the aortic areas. An electrocardiogram showed slight myocardial damage.

It is the opinion of the members of the department of cardiology that although the patient has a rheumatic heart there is probably syphilitic involvement of the aorta. Serologic examination gave 100 per cent positive results.

DISCUSSION

DR. E. A. OLIVER: This case is interesting and instructive. The unusual feature is the extensive and rapid development of the nodulo-ulcerative lesions to cover such a large area in nine months. This is probably due to the fact that the patient has an acute cardiac involvement, is ill and of course offers little resistance to the disease. His antisyphilitic therapy must be carefully supervised.

DR. A. W. STILLIANS: The cardiac lesion may be malignant, but I question the propriety of applying that term to the syphilis.

DR. THEODORE CORNBLEET: I have observed two or three cases at the Cook County Hospital which proved to be instances of a malignant type of gummatous syphilis, in that specific treatment was of little help until high caloric diets were given to relieve a state of inanition. I believe there is a parallel in this case. This patient will probably have to receive not only antisyphilitic treatment but therapy directed against his cardiac disease before his syphilis shows maximal improvement.

DR. WILLIAM ALLEN PUSEY: May I offer a criticism of the term malignant syphilis in a case of this sort? That term should be carefully limited to syphilis which is not amenable to specific treatment. It is now used commonly simply to indicate severe involvements. According to a pretty large experience in the old days, malignant syphilis was extremely rare, and I do not believe this case should be designated as one of malignant syphilis.

Sarcoid. Presented by DR. E. A. OLIVER and DR. W. W. TOBIN (by invitation).

This patient, a Negress aged 53, states that she has had an eruption on the face for twenty-five years. The eruption began on the left cheek as small red lumps, and these have gradually multiplied. Later, new areas appeared on the forehead and in the scalp. Radiation and ointments were used in the early days of treatment but to no avail. In 1931 she received radium treatments on the left cheek. These caused some improvement but resulted in scarring. For the past six months there has been an ulcerated lump on the lower part of the left cheek.

When first seen the patient presented an eruption of grouped dark red firm papules and nodules on the left side of the face, extending from the forehead over the mandible; at its lowermost portion diffuse whitish scarring had occurred. Similar areas without scarring were present on the forehead and on the right frontal area. There was an ulcerated, nodular, hard lesion, the size of a nickel, in the scar tissue on the lower part of the left cheek. This lesion was diagnosed clinically as epithelioma and was removed by electrocoagulation.

Serologic examination gave a negative result. The reaction to tuberculin with 0.1 cc. of a dilution of 1:1,000 of Koch's old tuberculin was positive. A roentgenogram of the chest showed old healed apical tuberculosis.

Histologic examination showed circumscribed nodules separated by connective tissue septums which consisted almost entirely of epithelioid cells and a few plasma cells and giant cells. The epidermis was markedly thinned and the interpapillary prolongations obliterated.

DISCUSSION

DR. M. H. EBERT: At the last meeting I presented a case of sarcoid of the Besnier-Boeck-Schaumann type, a clinical entity that is different from the condition in the case under observation today. It is a systemic disease which has manifestations on the skin, in the bones and the lungs and, frequently, on the mucous membrane. In cases of this type the reaction to tuberculin is almost invariably negative, and the condition responds poorly to treatment. There is a good deal of dispute among European authorities as to the nature of the disease.

Some say it has no relation to tuberculosis and others that it is a hematogenous tuberculous infection on a soil which responds in this peculiar fashion. The case presented today is of a variety of sarcoid which is seen among American Negroes —hematogenous tuberculosis on that particular soil. Dr. Nomland has presented several cases in which the picture resembled this one. In these the tuberculin reaction at times has been positive and at times negative. I remember one case in which the reaction was negative for a time and then became positive. This condition in the Negro is often associated with open tuberculosis in other parts of the body. As the members know, ordinary sarcoid does not ulcerate, but these lesions may break down and ulcerate. The histologic picture is somewhat different. Some of the members saw the slide I presented last month, of a sharply delimited group of epithelioid cells, few lymphocytes and no other tissue reaction. The histologic picture in the case today would suggest an atypical tuberculoid reaction which might be interpreted as lupus vulgaris. If both pictures represent tuberculosis, they are tuberculosis in persons with different processes of immunization. The reaction to tuberculin in this case was positive.

Dr. Hamilton Montgomery, Rochester, Minn.: The picture of various forms of sarcoid in Negroes is complex, and different ideas have been expressed in the literature. In many of the cases histologically there is marked caseation necrosis, and the histologic picture thus corresponds to that of tuberculosis cutis follicularis disseminatus (lupus miliaris disseminatus); the condition in Negroes was originally so classified by Wise and Sulzberger. In other cases, such as this one, there is no caseation necrosis but chiefly epithelioid cells with a few giant cells and lymphocytes—in other words, the histologic picture of sarcoid. A positive reaction to the tuberculin test is usually not found in cases of sarcoid, but this does not rule against this diagnosis.

Dr. W. W. Tobin (by invitation): The epithelioma has been present for six months. It occurred in the scar tissue, which was not present until after roentgen therapy was given in 1931, and was probably on the basis of a radium dermatitis rather than a sequel to sarcoid.

Dr. William Allen Pusey: I should like to repeat that I have seen epithelioma develop in cases like this in which roentgen therapy had not been employed.

A Case for Diagnosis (Eczematoid Eruption). Presented by Dr. Theodore Cornbleet.

C. H., a man aged 32, noticed a pruritic papular eruption on the inner surface of the left calf about eight months ago. Within three months the lesions spread to both legs and a month later to the abdomen. Salves of various kinds were applied but no good result followed.

Eleven months ago, while the patient was in the Cook County Hospital with bronchopneumonia, a small abscess developed on the sternum, which since that time has grown to the size of a small grapefruit. This has not caused pain or inconvenience until the present time.

Physical examination shows a fading congested erythema on the cheeks and the nose. Two weeks ago this resembled acute disseminated lupus erythematosus. On the trunk and the extremities chronic scaly, sharply defined, elevated patches of dermatitis are seen; in addition, there are bullous formations on the legs. The shoulders and the buttocks are relatively free. There is a large tumor protruding over the sternum. At the present time it is painful and tender.

A roentgenogram of the chest showed bilateral increase of the hilar markings; fluoroscopic examination showed no abnormality.

DISCUSSION

Dr. F. E. Senear: I think the picture on the legs, the trunk and the arms is, on the whole, rather nondescript, but generally I should say most of those lesions would fit in rather well with the common conception of infectious eczematoid dermatitis. On the legs, where the dermatitis is more diffuse and more dis-

tinctly of the patchy type, it suggests a simple hypostatic dermatitis. I think all dermatologists see patients who have dermatitis on the legs for a considerable time and then undergo development, in a more or less explosive fashion, of eczematous lesions on other parts of the body. I have watched such patients for a number of years and have felt that probably the type of generalized eruption seen as the secondary manifestation might be classed as belonging to the "id" group, possibly in some instances as bacterid and in others as eczematid. In accordance with the work of Rasch and Whitfield, these secondary eruptions may be conceived to be due to sensitization of the patient to his own metabolic products. Many years ago Dr. Pusey called attention to the fact that in the later years of life there is sometimes a decided tendency to the formation of bullous lesions on the lower extremities in types of eruption that would not ordinarily be considered bullous. I think bullae of the type present on the legs of this patient can be explained as belonging to that group. With regard to the lesion in the sternal region, I have nothing to say, except that in view of the negative serologic reaction a therapeutic test might be indicated.

DR. THEODORE CORNBLEET: I am grateful to Dr. Senear for his remarks. I did not feel that the lesion on the chest was related in any way to the eruption, but I wanted to make sure by fluoroscopic and roentgen examination that there was not mediastinal Hodgkin's disease. The cutaneous eruption on such a basis could be a Hodgkin id. I could not account for the bullous formation on the legs in association with this generalized patchy crusted eruption. All the possibilities have not been exhausted in the hunt for an infecting organism, but scrapings have shown no fungi. The possibility that a drug—perhaps bromide—might be responsible for the eruption was considered. The possibility of Duhring's disease was thought of because of the marked grouping of the lesions, but the pruritus has not been severe enough, and there is no eosinophilia. The eruption is difficult to classify and makes one invoke such poorly defined and inclusive groupings as the "ids."

Actinomycosis. Presented by DR. THEODORE CORNBLEET.

G. C., a boy aged 11 years, was admitted to the Cook County Hospital on Oct. 19, 1937. There was nothing significant in the family or the personal history. About three months ago the patient experienced difficulty in passing urine, and the amount was scanty. There has been loss of weight. About a week ago enlargement of the lower part of the abdomen became evident, and some pain was present.

Physical examination shows a palpable mass about the size of an orange, extending from the umbilicus to the symphysis directly in the midline. This mass is firm and hard and is attached to the anterior abdominal wall. The point of tenderness is 1 inch (2.5 cm.) below the umbilicus. There are palpable inguinal lymph nodes, varying in size from that of a pea to that of a marble. The urine showed many erythrocytes. The leukocyte count was 14,400. A roentgenogram of the chest showed a bilateral increase in hilar markings; that of the abdomen and the pelvic bones showed no pathologic structure.

A diagnosis was made of cyst of the urachus, and operation was performed Nov. 9, 1937. Several ounces of thick pus was obtained. Two sinuses now extend through the linea alba and connect with the tract which extends from the umbilicus toward the bladder. There are no signs of intraperitoneal involvement.

Histologic examination showed actinomycoses of the wall of the abdominal abscess.

DISCUSSION

DR. E. A. OLIVER: This interesting case recalls to me a good article on the treatment of actinomycosis by O. H. Wangensteen (Role of Surgery in Treatment of Actinomycosis, *Ann. Surg.* **104**:752 [Oct.] 1936). The author expressed the beleif, after an experience of many years with medication with

potassium iodide, with irradiation and with surgical methods in the treatment of actinomycosis, that operative procedure is the agent of greatest value. In his opinion it is the most direct way to attack the disease. The reason for this lies in the fact that the infection is anaerobic, and removal of the dead tissue, which is poorly oxygenated and an excellent culture medium, will usually terminate the disease.

The prognosis in cervicofacial actinomycosis, he stated, is good, unless too much reliance is placed on the administration of potassium iodide and irradiation. These procedures, he said, are in no sense specific and do not warrant—especially the former—the confidence that is generally placed in them.

Dr. Otto H. Foerster, Milwaukee: I think all the members know that in a small number of cases of actinomycosis the appendix is the primary focus and that involvement of other parts, particularly the abdominal wall, is secondary. About twenty-five years ago I saw a young woman whose abdomen was riddled with 20 sinuses. Her weight was reduced to about 70 pounds (32 Kg.), but she recovered after treatment with roentgen rays, iodides and copper sulfate and is still living.

Dr. William H. Goeckerman, Los Angeles (by invitation): During the years that I was associated with the Mayo Clinic I observed a number of cases of deep-seated actinomycosis, and the surgeons always refused to do surgical intervention. So far as the use of potassium iodide is concerned, my associates and I pushed it to enormous doses, and I have never seen the condition improve as a result of its administration. I am excluding cases in which the condition involved the jaws and the neck. In two cases I observed recently I tried to get a surgeon interested, and he refused to operate. I wonder if the article referred to has changed the opinion of surgeons somewhat. Certainly it would seem that, if any results are expected, they have to be obtained through the cooperation of surgeons.

Dr. Theodore Cornbleet: I think the surgeons felt that they had by no means removed all the diseased tissue. The idea Dr. Oliver mentioned might be of use in this particular patient, because there is an opening in the abdomen from which secondary sinuses could be made into the infected tissues. Instead of allowing the air to enter passively, oxidizing materials could be injected into these prepared sinuses.

MINNESOTA DERMATOLOGICAL SOCIETY

John F. Madden, M.D., *President*

Oct. 22, 1937

F. W. Lynch, M.D., *Secretary*

A Case for Diagnosis (Lupus Erythematosus?). Presented by Dr. Harry Garfield Irvine and Dr. D. D. Turnacliff, Minneapolis.

For the past three years this man has had recurrent flare-ups of swelling over both cheeks and the nose, accompanied with chills and fever. Between attacks a thickening persists, which gives an appearance similar to scleroderma. The teeth and sinuses have shown no sign of infection.

Diagnoses of acute lupus erythematosus, recurrent erysipelas, rosacea, tuberculid and dermatitis from glasses have been considered. Bismuth and roentgen therapy have perhaps had a palliative effect.

Our opinion is that the condition is the type of lupus erythematosus which will flare up with more extended lesions. Should sulfanilamide be tried?

(Microscopic slides were shown.)

DISCUSSION

DR. JOHN F. MADDEN, St. Paul: This condition probably is cellulitis accompanying some inflammatory condition of the nose. I have seen similar reactions in association with acute rhinitis and sinusitis.

Dermatitis Due to Quinidine Sulfate. Presented by DR. JOHN F. MADDEN, St. Paul.

Mr. E. F., aged 48, has had syphilitic aortitis and has been under the care of a cardiologist who was giving him quinidine sulfate by mouth in addition to regular antisyphilitic treatment. After the patient had taken quinidine sulfate for four months irregular patches of acute vesicular weeping eczematous dermatitis, varying in size from that of a pea to that of an egg, appeared on the upper and the lower extremities about Aug. 1, 1937. The medication was discontinued for three weeks, and the eruption almost underwent involution (with no local treatment). On Sept. 1, 1937, the patient again began to take quinidine sulfate, and the eruption recurred in the same locations within forty-eight hours after the first tablet was taken. The recurrence was much more severe than the previous eruption. Patch tests with a 1 per cent solution of quinidine sulfate and a tablet of the same preparation such as the patient had taken were both negative at the end of forty-eight and seventy-two hours.

A Case for Diagnosis (Lichen Sclerosus et Atrophicus? Kraurosis Vulvae?). Presented by DR. JOHN F. MADDEN, St. Paul.

Mrs. P. B., aged 42, stated that she was well until January 1936, when she noticed an odorous thick yellow vaginal discharge. This was followed by pruritus and pain in the vulva. At the same time she noticed four pinhead-sized white macules on the left wrist and one on the right wrist. The pruritus has increased steadily. The labia now are studded with pinhead-sized white macules, associated with excoriations and atrophy of the labia minora.

Smears showed no gonococci or Trichomonas vaginalis. The Wassermann reaction was negative. The microscopic section showed changes in keeping with the diagnosis of lichen sclerosus et atrophicus.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester, Minn.: This case is definitely one of lichen sclerosus et atrophicus, and it is unusual to have the lesions limited to the vulva. There is no appreciable atrophy of the vulva for a woman of her age, and therefore I should not consider that there was any true kraurosis. Usually it is impossible to distinguish microscopically between lichen sclerosus et atrophicus and true kraurosis vulvae.

Parapsoriasis Variegata. Presented by DR. HARRY GARFIELD IRVINE and DR. D. D. TURNACLIFF, Minneapolis.

This patient, a man aged 50, had the first lesion on the thigh twelve years ago. Since that time more lesions have developed, and these have enlarged peripherally. The trunk and the thighs are about three-fourths covered with lesions of irregular size and shape that are characteristic of parapsoriasis variegata.

Microscopic sections were shown.

DISCUSSION

DR. L. H. WINER, Minneapolis: Clinically this patient shows atrophy, but the microscopic section does not show any atrophy. Microscopically the infiltrate is too cellular and dense for scleroderma. There is no change in the connective tissue. This condition, histologically, could be either typical idiopathic atrophy in an early stage or parapsoriasis. I favor the latter diagnosis.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I do not feel that clinically there is sufficient retiform arrangement of the lesions to justify the diagnosis of parapsoriasis variegata. There is a more marked degree of infiltrate in the sections than one usually sees in most forms of parapsoriasis. Histologically parapsoriasis is not specifically diagnostic. I believe the case belongs in the general broad group of parapsoriasis.

A Case for Diagnosis (Schamberg's Disease?). Presented by DR. CARL LAYMON, Minneapolis.

L. G., a Jew aged 50, stated that an eruption appeared on his legs in the spring of 1937 after injections into a ventral hernia. New lesions have continued to appear on the trunk and the upper extremities, despite local medication with various preparations. The pruritus was said to be severe. The patient's general health has remained good.

The patient seems to be in excellent health. The eruption is generalized but is most intense on the thighs and the legs below the knees. The lesions, which are not raised above the surface of the skin, are reddish brown plaques varying in size, on the borders of which are numerous tiny puncta. On the legs the skin seems diffusely stained brownish yellow. No excoriations are present.

The Wassermann test was negative; a histologic examination has not been made.

DISCUSSION

DR. W. GEORGE BROCK, Winnipeg, Canada (associate member): The generalized distribution, telangiectasia and pigmentation suggest to me Jacobi's type of poikiloderma. However, the patient claims the eruption began soon after a series of injections for the treatment of hernia. I should like to know what drug was used. The possibility of dermatitis medicamentosa might be entertained.

DR. RALPH RAYMOND SULLIVAN, Minneapolis: This case brings to mind the usual controversy attending the entire group of pigmentary dermatoses. I believe angioma serpiginosum should be considered and a biopsy made. This is a rather extensive involvement for Schamberg's disease, although I appreciate that cases have been reported in which the condition was generalized.

DR. CARL LAYMON, Minneapolis: What drug was injected into the hernia is impossible to determine. At one time the patient stated that he had a rash on his legs even before he had the injections. Some of the members have seen Touraine's recent monograph (Les capillantes en dermatologie, *Bull. Soc. franç. de dermat. et syph.* **44**:837, 1937). Touraine stated that Schamberg's disease could exist in a generalized form. He classified it under diseases due to chronic inflammation of the capillaries. The etiology remains unknown. Touraine classified under pigmented purpuric dermatitis all the various types of eczema and purpura of the legs in which stasis is apparently a factor. Pigmented purpuric lichenoid dermatitis of Gougerot and Blum was considered a special subtype, a classification which to me seems logical. The brownish red pigmentation, the telangiectatic puncta and the complete lack of lichenoid papules favor a diagnosis of Schamberg's disease in this case.

Ichthyosis Hystrix. Presented by DR. JOHN F. MADDEN, St. Paul.

Mr. E. Z., aged 42, states that his mother first noticed an eruption when he was 8 years old. The first lesions appeared on the knuckles and were soon followed by lesions on the palms and the soles. The eruption then spread to all parts of the body, gradually increasing in intensity during the first few hours of life. Since then it has remained practically the same, except that it is worse in the winter. So far as can be determined, no one in his family has had a similar eruption.

The eruption is more marked on the palms and the soles, where it is a diffuse thick hyperkeratosis. On other parts of the body there are thick hyperkeratotic lines and streaks associated with patches of dry, scaling, not appreciably thickened

skin. The hyperkeratotic streaks extend over the entire cutaneous surface except the face and are more marked in the flexures and the folds, such as the axillae, and the antecubital and popliteal spaces. The scalp is covered with a diffuse thick scale. The eruption was never moist and is asymptomatic.

The basal metabolic rate was + 14 per cent. The Wassermann reaction was negative. Microscopic section showed changes in keeping with the diagnosis of ichthyosis hystrix.

Ichthyosis. Presented by DR. H. E. MICHELSON and DR. CARL LAYMON, Minneapolis.

Mrs. S. A., aged 27, states that her present cutaneous condition first developed when she was about 1 year old. Her palms and soles became greatly thickened, scaly and fissured unless they were continually lubricated. Occasionally during hot weather vesicles would develop on her arms. Her mother and father are distantly related, but their skins are unaffected. The patient has two brothers and one sister who have a similar condition.

Examination of the skin shows the palms and the soles to be diffusely thickened and scaly. The skin of the dorsa of her hands and forearms is thickened and covered by horny papules. The skin on the flexor areas of the arms is more involved than that on the extensor surfaces, and in the popliteal spaces there are linear rows of horny papules. The skin of the legs is covered by large thick scales.

The Wassermann, the Kahn and the Kline test were negative.

(Histologic sections were shown.)

An Unusual Case of Ichthyosis. Presented by DR. CARL LAYMON, Minneapolis.

W. D. H., a man aged 30, states that his skin has been dry and red since birth. His general health is unaffected, and there seems to be no seasonal variation. The patient states that his father as a young man had a similar condition of the skin, which improved, however, after the age of 30. The patient has one sister, who has had no trouble with the skin.

The patient is a well developed man apparently in good health. The entire skin is erythematous, dry and somewhat scaly. The skin of the palms and the soles is thickened and hyperkeratotic. There is no special involvement of the popliteal and the antecubital spaces or the axillae. The skin on the legs seems more tense than normal and somewhat resembles that seen in superficial morphea. There is partial baldness of the scalp, not unlike that associated with pseudopelade.

The basal metabolic rate was —9 per cent.

(Histologic sections were shown. The changes were consistent with the diagnosis of ichthyosis.)

DISCUSSION ON ICHTHYOSIS

DR. CARL LAYMON, Minneapolis: To me the extreme thickening of the palms and the soles of the two patients just presented exemplifies Brocq's ichthyosiform erythroderma. The term is not a good one since erythroderma is not always present or may fade out as adulthood is reached. Likewise, bullae are not always found in this disease. The seborrheic involvement of the scalp and the thickening of the palms, the soles, the antecubital spaces and the axillae favor a diagnosis of ichthyosiform erythroderma. Ordinary ichthyosis, on the contrary, presents minimal involvement in these areas. It would simplify matters if the term ichthyosis hystrix were limited to circumscribed or linear verrucous nevi. In my patient, although the entire skin is erythematous, other features of ichthyosiform erythroderma are entirely lacking.

DR. H. E. MICHELSON, Minneapolis: I am greatly pleased to see Dr. Laymon's interest in the French school of dermatology, and I hope that he will soon be able to visit Paris. I think the confusion in this concept is largely a matter of nomenclature; according to the French point of view, this condition has one name, while according to a broader view, these cases may be grouped under the heading of ichthyosis.

Dermatitis Herpetiformis. Presented by Dr. H. E. Michelson and Dr. Carl Laymon, Minneapolis.

Mrs. H. G., aged 38, states that an eruption developed on the right side of her neck in August 1937. At that time she was confined to bed with bronchitis. During the next week the lesions spread rapidly and involved the axillae, the groin, the back and the area under her breasts. The lesions itched and burned and always started as blisters, which rapidly broke and crusted. While she was hospitalized for two and one-half weeks, the skin entirely cleared, as a result of application of an antiseptic lotion. For the past month, since her discharge from the hospital, the eruption has recurred, with symptoms of itching and burning.

Examination shows an obese woman with the neck, the axillae, the breasts, the groin and the scapular area involved with a cutaneous eruption. The primary lesion is a tense vesicle, and there are circinate and crusted lesions. Especially in the scapular and sacral regions and the axillae are numerous pigmented macules indicating the sites of previous lesions.

The Wassermann, the Kahn and the Kline test were negative.

Dermatitis Herpetiformis. Presented by Dr. John F. Madden, St. Paul.

Mr. H. K., aged 26, states that an eruption appeared in 1930 on the elbows, the knees and the sacrum and in the scapular region. The eruption is accompanied by severe pruritus. He has had remissions and exacerbations but has never been entirely well. The lesions appear in crops as papulovesicles, and many of them are followed by scarring and hyperpigmentation. The histologic picture was in keeping with the diagnosis of dermatitis herpetiformis.

DISCUSSION

Dr. S. E. Sweitzer, Minneapolis: If any of the members have access to an old atlas, they will find that the picture in the case of Drs. Michelson and Laymon is similar to the old illustrations of Duhring. Dermatitis herpetiformis is one of the things dermatologists had to study years ago using pictures instead of patients. And this picture looks much like the old illustrations.

A Case for Diagnosis (Scrofuloderma? Pyoderma?). Presented by Dr. John F. Madden, St. Paul.

Mrs. P. M., aged 35, a Mexican, states that she felt perfectly well until March 1937, when she noticed painless swellings in the right and the left anterior cervical region. These continued to enlarge until May 19, 1937, when they were incised. There have been ulcers, draining sinuses and cervical adenopathy since that time. The sinuses have always discharged seropurulent material. The nodules are extremely painful before they are incised or drain spontaneously. The patient knows of no member of her family who has had tuberculosis. When she was admitted to the hospital, it was evident that her personal hygiene was not good.

The Wassermann reaction was negative. Mantoux tests with dilutions of 1:1,000 and 1:10,000 gave negative results repeatedly. Roentgenograms of the chest showed no signs of pulmonary tuberculosis. Roentgen examination of the jaw showed no abscessed teeth or pathologic changes in the bones. The Frei test was negative. Examinations for ray fungi were repeatedly negative. The microscopic section showed a chronic inflammatory reaction with proliferation of epithelioid cells and was suggestive of tuberculosis.

DISCUSSION

Dr. Stephan Epstein, Marshfield, Wis. (associate member): I cannot remember having observed a case of scrofuloderma in which there was a negative reaction to a tuberculin test with a dilution of 1:1,000, but the negative reaction may not exclude that diagnosis absolutely.

DR. H. E. MICHELSON, Minneapolis: I think the patient has a colliquative type of tuberculosis. I do not believe the negative reaction to tuberculin is too conclusive, but in this type of tuberculosis the reaction usually is strongly positive.

Acute Perineal and Perianal Ulcers (Cause?). Presented by DR. JOHN F. MADDEN, St. Paul.

J. L., a girl aged 19 months, was first seen on Sept. 27, 1937. The patient's mother stated that on Sept. 20, 1937, she noticed what looked like a contusion covering the perineal and the perianal region. In about forty-eight hours the discolored area sloughed off and left sharply defined ulcers. When the patient was admitted to the hospital, these ulcers covered the perineum; two ulcers extended anteriorly over the labia, and one extended posteriorly, entirely encircling the anus. There was no history of trauma. The baby has never had a vaginal discharge. She was apparently well in the morning, and the first discoloration was noticed in the afternoon. There is a questionable history of diarrhea the day before the discoloration appeared. The ulcers have been healing steadily as a result of warm wet applications, and no new ones have appeared. The patient has no other eruption on the body.

Smears showed no gonococci or bacilli of Ducrey. No intestinal parasites were found. The Mantoux and the Wassermann reaction were negative.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: I observed a case this summer in which a family became infected with impetigo. The family physician treated them for a while. The little girl and the mother became infected with impetigo in the vaginal region, and the picture was like that in the case shown tonight. This condition might be a streptococcic lesion.

Pemphigus Vulgaris. Presented by DR. L. H. WINER, Minneapolis.

A Case for Diagnosis (Roentgen Dermatitis). Presented by DR. JOHN F. MADDEN, St. Paul.

Actinomycosis. Presented by DR. JOHN F. MADDEN, St. Paul.

Morphea. Presented by DR. JOHN F. MADDEN, St. Paul.

Pseudopelade. Presented by DR. JOHN F. MADDEN, St. Paul.

Lichen Urticatus. Presented by DR. JOHN F. MADDEN, St. Paul.

A Case for Diagnosis (Trauma to Nails). Presented by DR. H. E. MICHELSON, Minneapolis, and DR. F. T. BECKER, Minneapolis (by invitation).

Verruca Palmaris. Presented by DR. C. D. FREEMAN, St. Paul.

Erythroderma (Cause?). Presented by DR. JOHN F. MADDEN, St. Paul.

Granuloma Annulare. Presented by DR. JOHN F. MADDEN, St. Paul.

A Case for Diagnosis (Syringocystoma?). Presented by DR. JOHN F. MADDEN, St. Paul.

Pemphigus Vulgaris. Presented by DR. JOHN F. MADDEN, St. Paul.

A Case for Diagnosis (Recklinghausen's Disease?). Presented by DR. F. W. LYNCH, St. Paul.

Keratosis Follicularis (Two Cases, Involving Brother and Sister). Presented by DR. JOHN F. MADDEN, St. Paul.

JOHN F. MADDEN, M.D., *President*

Minneapolis, Dec. 2, 1937

F. W. LYNCH, M.D., *Secretary*

A Case for Diagnosis (Metastatic Carcinoma?). Presented by DR. H. E. MICHELSON, Minneapolis.

O. O., a man aged 54, was treated with roentgen rays for carcinoma of the prostate in December 1936 and in June 1937. Except for the need to urinate frequently he has felt well since. The nodule on the right side developed in September 1937.

Examination reveals a round firm erythematous nodule 1 cm. in diameter on the right flank.

Histologic sections have not yet been made.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: An unusual thing about the lesion is the marked tenderness or hyperesthesia, which is not usual in a metastatic lesion. A biopsy would seem essential to a diagnosis.

DR. CARL LAYMON, Minneapolis: When my associates and I first saw this patient, metastatic carcinoma and glomus tumor were considered in the diagnosis. On account of the firmness of the lesion and its location, we believed the possibility of glomus tumor was the less likely. We are planning to excise it for histologic study.

Static Ulcers. Presented by DR. S. E. SWEITZER, Minneapolis.

Two cases were presented to show the results of treatment by elevation.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: I am presenting these cases because there are so many of the same type and so much hospitalization is required. When the tremendous amount of edema subsides, the condition improves; so the first thing to do is get rid of the edema. This treatment saves a great deal of hospitalization.

DR. F. W. LYNCH, St. Paul: I have become convinced that the application of thioglycerol is of benefit in cases of chronic ulcers of the legs.

DR. ELMER M. RUSTEN, Minneapolis: The patient who had bilateral saphenous ligation indicates that this procedure is of value in controlling only that portion of the static dermatitis and crural ulcers caused by stasis in the saphenous vein. Treatment must be directed toward obliterating all varicosities. The recurrence of symptoms in this particular patient was due to patent varicosities arising from the popliteal vein.

DR. L. H. WINER, Minneapolis: These patients were presented because at the present time there are probably a dozen with similar lesions in the service with which I am associated. Because of the slow healing of the ulcers, it is necessary to hospitalize these patients for three months or longer. Dr. Sweitzer suggested that the leg be put up in a splint at an angle of 45 degrees. Subsequent to the elevation, healing has been rapid; within twenty-four hours the edema has disappeared, and by means of ordinary antiseptic packs (1:5,000 solution of potassium permanganate) the infection has been markedly reduced. One of the patients had ligations of the saphenous veins and injection into the veins previous to the ulcerations. No other treatment was given.

A Case for Diagnosis (Psoriasis? Lichen Planus?). Presented by DR. JOHN F. MADDEN, St. Paul.

This case is to be reported in detail at a later date.

DISCUSSION

DR. STEPHAN EPSTEIN, Marshfield, Wis.: I first had the impression of lichen moniliformis, but I have observed only Dr. Wise's case, in which the picture was not like this. In this case the lesions of the shoulder and the arms look much like lichen planus. The lesions of the face resemble lupus erythematosus. Lichen planus of the face is rare, but I recall a case at Jadassohn's clinic in which there were typical lichen planus of the body and lupus erythematosus-like lesions of the face.

DR. S. E. SWEITZER, Minneapolis: I am inclined to believe the condition is a form of lichen planus. This disease can be accompanied with scaling that looks like psoriasis.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Dr. Epstein mentioned lichen ruber moniliformis as the most likely diagnosis, and I would agree with him. I believe this condition is probably simply an earlier phase of that disease, as described recently by Dr. Wise. The histologic picture of lichen ruber moniliformis has no resemblance to that of lichen planus and therefore should establish the diagnosis in this case. Dr. Ormsby in his textbook distinguished lichen ruber moniliformis from lichen planus.

DR. H. E. MICHELSON, Minneapolis: In order to make a diagnosis of lichen ruber moniliformis, the condition must be defined. For my own part, I cannot decide that this condition is a disease apart from lichen planus. In this particular case I do not think a decision should be made until a biopsy specimen has been examined.

A Case for Diagnosis (Circinate Eruption). Presented by DR. H. E. MICHELSON, Minneapolis.

F. T., a man aged 61, had an eruption on the thighs five years ago (1932). After two years the lesions disappeared until the spring of 1936. Various types of local therapy have had but slight effect on the lesions. With the onset of cold weather the lesions improve a great deal.

The lesions at present are much less noticeable than they were during the warm summer months. The eruption now consists of two oval leukodermic areas on the anterior and the lateral surface of the right thigh. One is 15 by 22 cm., and the other is almost as large. During the height of the eruption the borders of the depigmented areas were made up of tiny bluish red papules resembling those of lichen planus. This feature of the eruption is at present almost entirely absent.

The Wassermann reaction was negative.

(Histologic preparations were shown.)

DISCUSSION

DR. L. H. WINER, Minneapolis: The section of the skin at the periphery of the lesion showed hyperkeratosis, dense round cell infiltrate in the upper part of the cutis and wiping out of the epidermal pegs. It corresponds with my concept of the microscopic characteristics of lichen planus.

DR. PAUL A. O'LEARY, Rochester, Minn.: I think the condition could be lichen planus.

DR. CARL LAYMON, Minneapolis: I thought the eruption was lichen planus until a biopsy specimen was taken. Either the lesion was missed or the condition is not lichen planus, since the histologic structure is not consistent with such a diagnosis.

Neurofibromatosis; Multiple Pedunculated Nevi or Verrucae. Presented by Dr. H. E. MICHELSON, Minneapolis.

E. S., a woman aged 47, has had an eruption since the age of 14. Her mother, one sister and one daughter have the same eruption. In the patient, as well as in the mother and the daughter, the lesions appeared at puberty.

Examination showed multiple soft pedunculated tumors in the axillae and the groins.

DISCUSSION

DR. CARL LAYMON, Minneapolis: It was my intention that the case be presented as one of neurofibromatosis. There is another interesting feature, i. e., the patient has a congenital abnormality of the spine resembling occult spina bifida. Her mother and her grandmother had a similar dermatosis, and in each instance the lesions appeared at the time of puberty.

DR. H. E. MICHELSON, Minneapolis: This particular form of lesion in the axillae and on the sides of the neck often has its onset during pregnancy, and some authors have ascribed to it a special place. The lesions can be destroyed easily by cautery.

Scleroderma Circumscriptum. Presented by DR. S. E. SWEITZER, Minneapolis.

S. B., a woman aged 48, states that a generalized eruption "like prickly heat" appeared in the middle of July 1937. The itching was intense, and she suffered from severe headaches. About a week later she noted that the skin over the left side of her neck and left shoulder was hard and felt "stiff." This manifestation spread from the left to the right side and somewhat inferiorly along the spinal column. Soon a patch developed on the left thigh, and several smaller areas appeared on the abdomen. The involved areas itched intensely. The itching, the size of the involved areas and the sensations of pressure have steadily progressed. Except for pulmonary tuberculosis in 1927, necessitating ten months of rest in bed, the patient's health has been excellent.

Examination shows an area on the back over which the surface of the skin appears smooth and has a yellowish white tinge. The skin in this area is tense and hard and cannot be picked up between the thumb and the forefinger. Several small lesions and a large one are present on the abdomen and the left thigh, respectively.

The histologic picture was consistent with a diagnosis of scleroderma.

Pemphigus Vulgaris. Presented by DR. S. E. SWEITZER, Minneapolis.

J. D., a man aged 56, states that an eruption appeared on his chest, back, scalp and arms in August 1937. New lesions rapidly appeared, until the process became practically generalized. The mouth was affected. The lesions seemed to start as "pimples," which soon became large blisters. The itching was intense. Except for the present condition, the patient's health has been excellent.

Examination shows the eruption to be generalized, including the palms and the soles. There are multiple eroded bullae in the mouth. The essential lesions are bullae, many of which are ruptured and covered with heavy crusts. The contents of many of the lesions are purulent. The lesions are especially numerous over the face and the sternum and between the scapulae.

The histologic picture was consistent with a diagnosis of pemphigus.

Acrodermatitis Chronica Atrophicans. Presented by DR. S. E. SWEITZER, Minneapolis.

J. H., a man aged 81, first noted redness and thinning of the skin on the hands early in 1937.

Examination shows the skin over the knees and the dorsa of the hands to be diffusely erythematous and extremely atrophic. There are bilateral varicosities.

Seasonal Contact Dermatitis. Presented by DR. S. E. SWEITZER and DR. ELMER M. RUSTEN, Minneapolis.

A. L., a man aged 51, states that he has had seasonal dermatitis for five years. The eruption appears in August and continues until the first frost. This year,

however, the eruption is still present. The dermatitis first appeared on the forehead but with each succeeding attack has become more extensive and now involves the forehead, the neck, the arms, the hands and the legs.

Physical examination reveals an eruption on the face, the hands, the arms and the legs, composed of inflammatory papules, discrete and grouped papulovesicles, lichenification, scaly crusts and excoriated points and lines.

Routine laboratory studies showed no abnormality. Patch tests with the pollen groups gave repeatedly negative results. A patch test with chrysanthemum coccineum gave positive results.

Pollen Dermatitis (Ragweed). Presented by Dr. S. E. Sweitzer and Dr. Elmer M. Rusten, Minneapolis.

J. B., a man aged 41, states that he has had pruritic seasonal dermatitis for the past eleven years. This eruption appears about August and continues until the first frost each year. Four years ago it persisted throughout the winter. The affected areas are the face, the neck, the hands, the arms and the legs.

His past health has been normal, except for dermatitis venenata involving the face twelve years ago, while he was in Denmark, and a "grain itch" involving the legs eleven years ago, shortly after emigration to this country.

Physical examination at this time shows no abnormality.

The routine laboratory examination showed nothing abnormal except for positive patch and scratch reactions to ragweed pollen.

DISCUSSION

Dr. Stephan Epstein, Marshfield, Wis.: I have made a similar observation. The patient had generalized dermatitis which presented the picture of atopic dermatitis on which subacute contact dermatitis was superimposed. He showed strongly positive reactions to the oily extracts of ragweed pollen, leaf and stem. The scratch test and the intracutaneous test with ragweed protein extract gave positive results, showing both an immediate reaction and a delayed reaction of the tuberculin type lasting over a week.

Dr. Elmer M. Rusten, Minneapolis: The two patients presented have a similar seasonal onset of symptoms, but the cause of the eruption and the duration of the disease differ. The patient with ragweed dermatitis is shown because of positive reactions to a patch test with the ragweed oil of pollen and to an intracutaneous test with the glycerin-soluble fraction of the same weed. I am of the opinion that this is uncommon. Specific treatment will be instituted with a pollen antigen and pollen oil.

Exfoliative Dermatitis (Psoriasis?). Presented by Dr. S. E. Sweitzer and Dr. L. H. Winer, Minneapolis.

M. L., a housewife 61 years of age, states that an eruption began in 1931, with redness and scaling of her hands. She used ointments locally, but during the next year the eruption gradually involved the entire body. As far as can be ascertained, the patient has never received arsenic in any form.

Examination shows the entire body to be involved. The skin is erythematous, thickened and covered with large scales. The scalp is covered with a thick tenacious scale. Bilateral ectropion is present. The cervical, axillary and inguinal nodes are small, hard and shotty. The finger nails are thickened and furrowed; the toe nails are greatly thickened and elongated, and all the nails show pitting.

The Wassermann, the Rytz and the Kahn reaction were negative.

DISCUSSION

Dr. H. E. Michelson, Minneapolis: I am inclined to feel that this particular form of psoriasis is distinct, although closely related to the arthropathic form.

The patient presents some signs which are suggestive of dermatomyositis. Treatment presents a real problem, and the prognosis is poor.

DR. S. E. SWEITZER, Minneapolis: This patient had what looked like tremendous atrophy of the heel, the body and the face.

Herpes Zoster. Presented by DR. S. E. SWEITZER, Minneapolis.

Eczema of the Hands, Aggravated by Zemo (with a Positive Reaction to Patch Tests with Zemo). Presented by DR. S. E. SWEITZER, Minneapolis.

Naevus Unius Lateris. Presented by DR. S. E. SWEITZER, Minneapolis.

Lupus Erythematosus. Presented by DR. H. E. MICHELSON, Minneapolis.

Ulcer of the Sole, Probably Artificial. Presented by DR. H. E. MICHELSON, Minneapolis.

A Case for Diagnosis (Rosacea?). Presented by DR. H. E. MICHELSON, Minneapolis.

Annular Sarcoid of the Forearm. Presented by DR. S. E. SWEITZER, Minneapolis.

Lupus Erythematosus. Presented by DR. CARL LAYMON, Minneapolis.

Vitiligo. Presented by DR. S. E. SWEITZER, Minneapolis.

MANHATTAN DERMATOLOGIC SOCIETY

ANDREW J. GILMOUR, M.D., *Chairman*

Nov. 9, 1937

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Rosacea-Like Tuberculid of Lewandowsky. Presented by DR. ANTHONY C. CIPOLLARO.

M. A., a woman aged 36, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in January 1936, complaining of an eruption of the face of six months' duration.

The patient states that about twenty years ago she had a primary lesion of syphilis for which she was treated, with an apparent cure. She states that she had an examination of the spinal fluid about ten years ago.

At present the patient presents many discrete erythematous papules over the forehead, the nose, the cheeks and the chin. The lesions spread to the preauricular areas. There is a diffuse redness in the involved areas. On diascopic pressure some of the papular lesions reveal small yellowish brown nodules.

To date she has received about ten injections of sodium gold thiosulfate and seven unfiltered fractional (75 r) roentgen treatments. These have brought no improvement. The reaction with dilutions of tuberculin 1:10,000, 1:100,000 and 1:1,000,000 was negative. The Wassermann reaction was negative. Examination

of the urine showed no abnormality. Microscopic examination of a lesion removed from the face showed a round cell infiltration. There was no histologic evidence of tuberculosis.

DISCUSSION

DR. J. FRANK FRASER: I cannot harmonize the microscopic picture with Lewandowsky's rosacea-like tuberculid. My diagnosis is rosacea.

DR. GEORGE M. MACKEE: I should not accept this case clinically as one of rosacea-like tuberculid of Lewandowsky, but there are features present that suggest it. Against that diagnosis is the fact that the disease has lasted approximately two years and there are no scars. Also, the eruption is in the center of the face. In favor of Lewandowsky's tuberculid are the papular lesions, but such lesions may occur in rosacea. Also in favor of the presenter's diagnosis is the negative reaction to tuberculin, which does not really mean much. Finally, a tuberculoid structure does not rule out rosacea. The stubbornness favors tuberculid but does not confirm the diagnosis. My tentative diagnosis is rosacea, but I suggest another histologic examination and a study of the papules with the diascope.

DR. ANTHONY C. CIPOLLARO: I realize that the histologic picture and the negative reaction to tuberculin militate against a diagnosis of rosacea-like tuberculid of Lewandowsky. This patient has a letter from Prof. Leopold Arzt in which that physician states that the patient had lupus miliaris disseminatus faciei. This diagnosis was confirmed by a microscopic examination. The patient was cured with roentgen therapy and sodium gold thiosulphate. She remained well for over a year. The condition at no time has behaved like ordinary rosacea. This patient has been treated with roentgen rays, sodium gold thiosulfate and white lotion since she has been under my care at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. This condition has persisted.

I did not question her about digestive disturbances. However, she is unstable emotionally. I have been endeavoring to obtain her consent to a thorough physical examination, including a study of the spinal fluid.

Lupus Miliaris Faciei. Presented by DR. ANTHONY C. CIPOLLARO.

A. M., a housewife aged 60, was presented by me at the last meeting of the Manhattan Dermatologic Society (ARCH. DERMAT. & SYPH. **37**:529 [March] 1938) with a diagnosis of lupus miliaris faciei. This was based mainly on the histologic report of two separate pieces of tissue removed at different times in a case of rosacea-like tuberculid of Lewandowsky. Clinically, the lesions which the patient presented resembled superficial basal cell epithelioma. A third biopsy specimen taken from a lesion on the cheek showed lupus erythematosus.

DISCUSSION

DR. DAVID L. SATENSTEIN: The fact that this patient might have rosacea-like tuberculid and lupus erythematosus is not so extraordinary. I have seen sarcoid and lupus erythematosus together.

DR. LUDWIG OULMANN: The important feature is not the coincidence of lupus miliaris and lupus erythematosus, which is known to all the members. At the last meeting some members regarded the one round lesion on the right cheek as an epitheliomatous lesion. This proved to be lupus erythematosus.

DR. DAVID L. SATENSTEIN: I have a patient at the clinic who gave a strongly positive reaction to tuberculin with a dilution of 1 : 1,000,000. The lesions responded to therapy up to a certain point, and there was no further improvement. Some one suggested a Wassermann test, which gave positive results, but there was absolutely no suggestion of syphilis.

DR. ANTHONY C. CIPOLLARO: I was unable to make a clinical diagnosis in this case and was further confused by the histologic reports obtained.

An Extensive Prickle Cell and Basal Cell Epithelioma; Results of Treatment. Presented by DR. PAUL E. BECHET.

E. G., a woman aged 52, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. She had a lesion on the right side of the forehead, extending from the eyebrow to the hair margin, in June 1921. It had been present for three years and measured about 7 or 8 mm. in diameter. It consisted of a large flat lesion with rolled borders and areas of superficial scarring. In its center was a cauliflower-like mass about 3 mm. in diameter and about 2 mm. in height, which was hard and had a marked indurated border. Sections of the flat lesion showed basal cell epithelioma, and the cauliflower-like mass showed prickle cell epithelioma. On June 29, 1921, the lesion was curetted with great thoroughness. An instrument of almost razor-like sharpness was used. The next day Dr. Howard Fox administered a single roentgen treatment, of 2¼ skin units (675 r), unfiltered. Thorough curettage and a single roentgen treatment were therefore the only therapeutic measures employed. She is shown sixteen years later, entirely well. The cosmetic results are excellent. She is exhibited to prove the value of the curet as an adjuvant in the treatment of epithelioma.

DISCUSSION

DR. JOHN REMER (by invitation): The result is really remarkable after sixteen years.

DR. ISADORE ROSEN: I believe it is important that all epitheliomas be thoroughly destroyed at the first operation, no matter what method is employed. Unless this is done, recurrences which may make it more difficult to treat the condition are apt to take place. In spite of any type of therapy, even surgical treatment, the disease involves the deeper structures. Dr. Bechet is to be complimented on the result he obtained in his case.

DR. GEORGE M. MACKEE: One of the most dangerous things regarding basal cell epithelioma is incomplete removal and a recurrence under the scar. If a recurrence takes place at the edge of the scar the patient is bound to recognize it. But if it recurs under the scar and the patient does not recognize it until later, it is difficult to eradicate.

DR. DAVID L. SATENSTEIN: I suggest that in all cases in which basal cell epithelioma is believed to be present the diagnosis be proved histologically before treatment is started. I have collected about 500 cases, and in a number of them the condition clinically was superficial. Microscopic examination, however, showed it to be of the infiltrating type. One cannot tell the infiltrating type by clinical appearance alone. All those lesions if they are at all extensive should first be taken out and examined, not so much to corroborate the diagnosis of basal cell epithelioma but to find out what it is doing and the depth of the lesion, because that information is of great value to the clinician in treatment.

DR. GEORGE C. ANDREWS: I think a biopsy should be done on every epithelioma. Every once in a while a case is observed in which a biopsy has not been made and the lesion has been treated as basal cell epithelioma. One or two years later there is a recurrence, and when histologic examination is done, squamous cell epithelioma is found.

DR. JOHN REMER (by invitation): Lately in treating epitheliomas I have been using a combination of filtered and unfiltered roentgen rays. I have been getting much better results this way.

DR. PAUL E. BECHET: This case was presented in order to demonstrate again the value of the curet in the treatment of epithelioma. The secret of success, in my opinion, lies in a sharp curet and in thorough use of it.

A Case for Diagnosis (Larva Migrans?). Presented by DR. J. FRANK FRASER.

A. S., a boy aged 2½ years, was previously presented at the October 1937 meeting of the New York Dermatological Society.

There is slight pruritus. On the buttocks, the abdomen and the back is an erythematous eruption arranged in pencil streak formation. The eruption began on the buttocks, spread to the abdomen and then to the back and is beginning to fade in the same order.

DISCUSSION

DR. FRED WISE: When I first saw the condition, a week ago, it was typical of larva migrans, and I still think it is that condition.

DR. GEORGE M. LEWIS: An unusual feature in this case is that the infestation was supposedly contracted at a local beach.

DR. MAX SCHEER: This is a rather unusual condition to get at the local beaches, but I have come across a few patients with the disease who said they had never been outside of New York or New Jersey. It may be that dogs who have been infected in Florida are the source of the infection at the beaches.

DR. ISADORE ROSEN: Since I did not see this patient before therapy was employed, it is difficult for me to make an absolute clinical diagnosis in the present stage of the disease. In the few cases that I have observed during the past twenty or more years in the city of New York there have been clinical features which differed from those in this patient. The local inflammatory reaction was definite in all, and there was distinct vesiculation in some of the involved areas, especially in the advancing portion of the lesion. I do believe, however, that in the case under discussion the condition is of parasitic origin.

DR. GEORGE M. MACKEE: I agree with the diagnosis of creeping eruption.

DR. GEORGE C. ANDREWS: I have observed few cases of this disease, but in those that I did observe there were coarser tunnels. There is no vesiculation evident in this case.

DR. PAUL E. BECHET: At the previous presentation I considered the eruption a typical example of "creeping eruption" and gave my reasons for this opinion. While the eruption has to a certain extent changed its appearance since that time, it is still typical of that disease.

DR. GEORGE M. LEWIS: The parasite may be demonstrated by removal with a needle or in histologic section.

Verrucous Nevus, Systematized. Presented by DR. GEORGE C. ANDREWS.

C. K., a girl aged 6 years, presents a widespread eruption which appeared a few months after birth. It consists of follicular keratotic papules that have coalesced to form diffused horny patches. These are scattered in linear streaks and distributed fairly symmetrically over the arms, the legs and the loins. The involvement is particularly severe in the axillae, where thick verrucous folds are present. The mother states that three years ago the eruption completely disappeared after peeling from severe sunburn but that it soon recurred. Histologic examination showed focal papillary proliferations of the epidermis, with marked hyperkeratosis and acanthosis. The epidermal cells showed a spongy degeneration. There were no abnormal deposits of melanin. The patient has been treated by injections of liver extract and by fractional roentgen treatments, limited to one small area. There has been no improvement.

DISCUSSION

DR. PAUL E. BECHET: I think that this patient presents the typical picture of ichthyosis hystrix. Whether or not this is a nevus has not as yet been definitely determined.

DR. GEORGE M. MACKEE: There is no sharp demarcation between certain nevi and congenital keratoderma. This condition used to be called ichthyosis hystrix, and now it is called systematized verrucous nevus.

DR. GEORGE C. ANDREWS: I had the impression that the term ichthyosis hystrix was gradually being discarded. The point that was interesting to me in this case was the differential diagnosis from acanthosis nigricans of the juvenile type.

Psoriasis. Presented by DR. GEORGE M. LEWIS.

N. J., a man aged 30, a florist, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He has had an eruption on his hands for the past five years. There has never been any vesiculation. Roentgen therapy, given elsewhere, effected slight improvement but was discontinued after two or three treatments. The palms and the flexor surfaces of the fingers show an erythematous, dry and thickened patchy eruption. A number of fissures are present in the affected skin. No other evidence of the disease is found. Patch tests with suspected irritants gave negative results. The histologic diagnosis was psoriasis.

DISCUSSION

DR. GEORGE C. ANDREWS: In spite of the fact that the histologic picture is that of psoriasis, I believe that since the patient is a florist, he should have a thorough examination of the urine and the blood for arsenic. His occupation exposes him to arsenic, and the lesions on the palms are not unlike arsenical eczema. On the left palm there are several dark keratotic lesions which somewhat suggest arsenical origin. The histologic diagnosis of psoriasis in cases in which the picture is atypical is not reliable.

DR. DAVID L. SATENSTEIN: I believe that if this patient's hands are bandaged for about a week, without washing or any applications, a more characteristic picture of psoriasis will present itself than that evident tonight.

DR. ISADORE ROSEN: I agree with the diagnosis as presented. The clinical features, which are erythema, scaliness and sharpness of outline, strongly suggest the diagnosis of psoriasis. Arsenical keratoses show much less inflammatory reaction and are persistent.

DR. PAUL E. BECHET: I agree with the diagnosis as presented. The patches are sharply marginated. On the ball of the thumb there is a healthy area of skin, immediately adjacent to the patch. The color of the lesions is typical of psoriasis. The patches are scaly, and I observed striae and pits on the finger nails. Even on the backs of the fingers the eruption is clearly outlined. I have observed several instances in which the lesions of psoriasis were confined to the hands.

DR. GEORGE C. ANDREWS: I looked carefully at all the finger nails. I could not see any pits or other signs of psoriasis there. The patient has no psoriasis on any other part of his body, nor is there a history of psoriasis either in himself or in his family. The eruption, in my mind, is possibly an eczematous eruption due to arsenic. The acceptance of the diagnosis of psoriasis means that this man, with the usual treatment for that eruption, will have this condition more or less for the rest of his life. It is only fair to the patient to give him the benefit of any possible doubt and perform tests for arsenic.

DR. GEORGE M. LEWIS: The sprays which he has used contained no arsenic. The spray he is using at present contains pyrethrum. He does not use fertilizer in his work or come in contact with any. There is no history of ingestion of arsenic. Nevertheless I shall try to follow the suggestion of Dr. Andrews.

Pityriasis Varioliformis Acuta. Presented by DR. LUDWIG OULMANN.

V. S., a boy aged 14, presents an eruption which developed several days before his first appearance, which was one week ago. There were a slight chill and malaise at the time of the onset. The eruption is generalized on the trunk, the face and the extremities and consists of maculopapular lesions varying in size

from that of a pinhead to that of a lentil. Some of the lesions show tiny ulcerations, and others are lichenoid. Some are scaly. There is a grouping of these tiny moist papules around both axillae. The cervical and the inguinal glands are swollen to the size of a pea or a bean. The eruption is typical for this diagnosis. The mucous membrane of the mouth is not affected; there are no history of fever and no subjective symptoms. During the past week, while the patient was under observation, new lesions have appeared. This patient has taken no drugs within the past six months.

DISCUSSION

DR. FRED WISE: I agree with the diagnosis without any qualifications. As far as the short duration is concerned, that is where the word acuta originated in connection with the eruption.

Pyoderma. Presented by DR. GEORGE M. LEWIS.

W. L., a man aged 22, a stock clerk, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in September because of a sore on the left cheek, near the mouth, of three months' duration. The lesion has enlarged slowly.

An apparently boggy or infiltrated inflammatory lesion is present on the left cheek at the angle of the mouth. There are small follicular pustular lesions on the left cheek and the neck. The Wassermann reaction was negative. The reaction to trichophytin was negative. Repeated examinations failed to demonstrate fungi. The white blood count was 11,400, with a normal differential count. The urine was normal. The histologic picture showed an irregularly acanthotic epidermis, with interstitial edema and in parts a little parakeratotic horny layer. The superficial vessels were dilated, and there was a diffuse infiltrate of small round cells, connective tissue cells and some polymorphonuclear leukocytes. The histologic diagnosis was chronic eczema.

DISCUSSION

DR. DAVID L. SATENSTEIN: I should like to ask Dr. Wise what he will do if this condition does not respond to roentgen rays. Often similar lesions on the legs do not respond to roentgen rays.

DR. FRED WISE: In answer to Dr. Satenstein, if this condition does not respond to roentgen rays, I shall curet the lesion.

DR. GEORGE M. LEWIS: This man has been under observation for the past few weeks, during which time I have been attempting to make a definite diagnosis. My investigation has not been fruitful, and the diagnosis of pyoderma has been arrived at mainly by exclusion. I plan now to begin roentgen therapy.

Book Reviews

A Practical Treatise on Diseases of the Skin for the Use of Students and Practitioners. By Oliver S. Ormsby. With Revision of the Histopathology and Mycology by Clark Wylie Finnerud. Fifth edition. Price $12. Pp. 1,334, with 658 engravings and 3 colored plates. Philadelphia: Lea & Febiger, 1937.

Clear, concise and systematic, this book at once covers the fundamentals of dermatology and branches out to other fields which are of special interest to the dermatologist. The book is too well known to justify an attempt at a résumé. The classification of its contents has been admirable. By means of it each subject or individual disease may be found easily and quickly in its proper relation to the text. The chapters on general etiology, diagnosis and prognosis avoid duplication and give the reader a quick and thorough grasp of the material he wishes to study. The chapters on syphilis, tuberculosis, mycotic infections and especially blastomycosis may be singled out as outstandingly excellent. The section on histopathology and mycology has been written by Dr. Clark W. Finnerud, to whom Dr. Ormsby has given proper credit. It is gratifying that the author has presented the differential diagnosis of the exanthems from other dermatologic conditions for which they are often mistaken by nondermatologists. Most other dermatologic textbooks give scant attention to this group of diseases. The bibliography has been carefully prepared and brought up to date. The illustrations which fill the volume are excellent.

The text is not free from the faults found in all books of its kind. Much more space is given to the treatment of diseases than the actual value of the subject warrants. Many prescriptions are listed which differ but slightly in composition. In the section on acne vulgaris relatively little space is given to radiotherapy, which is the most effective single method of treatment for this disease. It is this reviewer's opinion that the greater part of the space devoted to the discussion of the subject and the presentation of familiar material is of little value. Surprisingly little space is given to the discussion of chancroid, a disease which is much more frequent than blastomycosis, to which several pages are devoted.

The great labor involved in revising this text and the excellent results obtained are a credit to the author.

Who Gave the World Syphilis? The Haitian Myth. By Richmond C. Holcomb. Price, $3. Pp. 189. New York: Froben Press, Inc., 1937.

In this book Capt. Richmond C. Holcomb, Medical Corps, United States Navy, takes exception to the theory of the American origin of syphilis. After securing a photostat from the single copy in the United States, owned by the Huntington Library in San Marino, Calif., of the celebrated work of Ruiz Diaz de Isla, the principal authority on the Haitian origin of syphilis, he carefully analyzes the work. He states that it reveals many contradictions. The evidence does not support the prevailing view that the book was written before 1520. Also fallacious is the statement that Columbus sailed his two surviving caravels to Barcelona, Spain, on his return from the first voyage of discovery. The facts attest that he landed at Palos de la Frontera, Spain, on March 15, 1493, and went overland to Barcelona to make his report to the king and queen. He did not take any of his men, but six Indians, all men, accompanied him. This sets at rest the legend that he brought back women, who were taken to Naples and there spread the disease. The records of Columbus' first voyage definitely prove that he and his companions returned to Spain in an apparently healthy state. The statement that Martin Alonzo Pinzon had syphilis and was treated by de Isla at Barcelona in 1493 is,

in the words of Captain Holcomb, "a scandalous interpolation without support in either evidence of circumstance in time, place, or person." The so-called siege of Naples is a myth. According to Commines, who accompanied Charles VII, the French army was warmly received by the Neapolitans and entered the town on Feb. 22, 1495, having left Capua, Italy, four days previously. Holcomb believes Sudhoff is correct in the opinion that the epidemic among the French soldiers left at Atessa, Italy, when Charles returned home was one of typhoid fever and not one of syphilis. The expulsion of the Jews from Spain in 1492, well under way before Columbus began his voyage of discovery, spread epidemics of plague, typhoid and typhus, which were later ascribed to and confused with the so-called new disease.

De Isla was extremely fond of using guaiacum, the holy wood, in the treatment of syphilis. As this product was of Haitian origin, de Isla stated that the remedy was given to the inhabitants of the West Indies by Divine providence and that the disease originated there as a punishment for sin. It is possible that this statement might have been made by him to support his views as to the specificity of guaiacum in syphilis and that he had no real scientific basis for it.

Arsenicodermie. By Robert Simons. Pp. 140. Leyden, Netherlands: A. W. Sijthoff, 1937.

This comprehensive monograph is based on the author's personal observations of 200 patients and a critical review of more than 1,000 cases in the literature. It opens with a discussion of the general symptoms of arsenical intoxication. The author objects to the term "arsenical intoxication" in cases in which the symptoms disappear spontaneously. He cites the frequent occurrence of diarrhea, conjunctivitis and herpes zoster and their spontaneous disappearance during the continued administration of arsenic.

He discusses arsenical tolerance and states that it is greater in children than in adults. The effect of the drug on each organ and the arsenical content of the bodily secretions are discussed. The involvement of the nervous system occurs through (1) the arsenical effects as such (permeability); (2) the influence on the capillaries, such as hyperemia or anemia following hyperemia of the splanchnic viscera; (3) autointoxication following arsenical involvement of one of the viscera. He points out that arsenic may be present in the urine of normal persons who are exposed to this metal through environment, occupation or diet. The arsenical content may vary according to geographic location. For a given locality the author advises a determination of what he calls "a pseudo-normal index," which must be taken into consideration when determinations of arsenic are interpreted.

The erythematous changes, he believes, are produced primarily through capillary alterations. Under the heading of erythematous changes he discusses erythema, purpura, hyperhidrosis, furunculosis, urticaria, erythema multiforme, herpes zoster, edema, arsenical pemphigus, conjunctivitis, urethritis, mastitis, stomatitis and other forms of involvement of the mucous membranes.

Separate chapters are devoted to a discussion of arsenical melanosis and leukoderma, of hyperkeratosis and of carcinoma. Appended photographs illustrate these topics.